



Supporting Information

for

Synthesis of tricyclic fused pyrrolidine nitroxides from 2-alkynylpyrrolidine-1-oxyls

Mark M. Gulman, Yuliya F. Polienko, Sofia Yu. Trakhinina, Yuri V. Gatilov,
Tatyana V. Rybalova, Sergey A. Dobrynin and Igor A. Kirilyuk

Beilstein J. Org. Chem. **2026**, 22, 344–351. [doi:10.3762/bjoc.22.22](https://doi.org/10.3762/bjoc.22.22)

Experimental protocols, copies of the ^1H NMR, IR and EPR spectra and X-ray analysis data

Table of contents

Experimental procedures.....	S4
General method of the synthesis nitroxides 2d,e via reaction of nitron with alkynylmagnesium bromide	S4
2,2,5-Triethyl-3,4-bis(hydroxymethyl)-5-((trimethylsilyl)ethynyl)pyrrolidin-1-oxyl (2d).....	S5
2-(3-(Benzyloxy)prop-1-yn-1-yl)-2,5,5-triethyl-3,4-bis(hydroxymethyl)pyrrolidin-1-oxyl (2e).....	S5
2-(3-(Dimethylamino)prop-1-yn-1-yl)-2,5,5-triethyl-3,4-bis(hydroxymethyl)pyrrolidin-1-oxyl (2f)...	S6
General method of mesylation of nitroxides	S6
2,2,5-Triethyl-5-ethynyl-3,4-bis(((methylsulfonyl)oxy)methyl)pyrrolidin-1-oxyl (3a).....	S7
2,2,5-Triethyl-3,4-bis(((methylsulfonyl)oxy)methyl)-5-(phenylethynyl)pyrrolidin-1-oxyl (3b).....	S7
2,2,5-Triethyl-3,4-bis(((methylsulfonyl)oxy)methyl)-5-(3-((methylsulfonyl)oxy)prop-1-yn-1-yl)pyrrolidin-1-oxyl (3c).....	S7
2,2,5-Triethyl-3,4-bis(((methylsulfonyl)oxy)methyl)-5-((trimethylsilyl)ethynyl)pyrrolidin-1-oxyl (3d)	S8
2-(3-(Benzyloxy)prop-1-yn-1-yl)-2,5,5-triethyl-3,4-bis(((methylsulfonyl)oxy)methyl)pyrrolidin-1-oxyl (3e).....	S8
2-(3-(Dimethylamino)prop-1-yn-1-yl)-2,5,5-triethyl-3,4-bis(((methylsulfonyl)oxy)methyl)pyrrolidin-1-oxyl (3f).....	S8
General method for the synthesis of tricyclic fused triazole derivatives.....	S9
6-(Azidomethyl)-3b,5,5-triethyl-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2-c][1,2,3]triazol-4-oxyl (4a)	S9
6-(Azidomethyl)-3b,5,5-triethyl-3-phenyl-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2-c][1,2,3]triazol-4-oxyl (4b).....	S9
3,6-Bis(azidomethyl)-3b,5,5-triethyl-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2-c][1,2,3]triazol-4-oxyl (4c)	S9
6-(Azidomethyl)-3b,5,5-triethyl-3-(trimethylsilyl)-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2-c][1,2,3]triazol-4-oxyl (4d).....	S10
6-(Azidomethyl)-3-((benzyloxy)methyl)-3b,5,5-triethyl-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2-c][1,2,3]triazol-4-oxyl (4e)	S10
6-(Azidomethyl)-3-((dimethylamino)methyl)-3b,5,5-triethyl-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2-c][1,2,3]triazol-4-oxyl (4f).....	S10
3,4-Bis(acetoxymethyl)-2,2,5-triethyl-5-ethynylpyrrolidin-1-oxyl (5).....	S10
General method for the synthesis of alkynones.....	S11
3,4-Bis(acetoxymethyl)-2,2,5-triethyl-5-(3-oxo-3-phenylprop-1-yn-1-yl)pyrrolidin-1-oxyl (6a)	S11
3,4-Bis(((methylsulfonyl)oxy)methyl)-2,2,5-triethyl-5-(3-oxo-3-phenylprop-1-yn-1-yl)pyrrolidin-1-oxyl (6b)	S11
2,2,6a-Triethyl-3-(hydroxymethyl)-1-6-(2-oxoethylidene)hexahydro-1 <i>H</i> -furo[3,4- <i>b</i>]pyrrol-1-oxyl (8)	S11
2,2,5-Triethyl-3,4-bis(hydroxymethyl)-5-(5-phenyl-1 <i>H</i> -pyrazol-3-yl)pyrrolidin-1-oxyl (9a)	S12

Annulated tricyclic pyrazole derivatives synthesis	S12
3b,5,5-Triethyl-6-(((methylsulfonyl)oxy)methyl)-2-phenyl-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2- <i>b</i>]pyrazol-4-oxyl (9b)	S13
3b,5,5-Triethyl-6-(hydroxymethyl)-2-phenyl-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2- <i>b</i>]pyrazol-4-oxyl (9c).....	S14
NMR spectra	S15
Figure S1. ¹ H NMR (300 MHz, CD ₃ OD, Zn/CF ₃ COOH) of 2,2,5-triethyl-3,4-bis(hydroxymethyl)-5-((trimethylsilyl)ethynyl)pyrrolidin-1-oxyl (2d).....	S15
Figure S2. ¹ H NMR (300 MHz, CD ₃ OD, Zn/CF ₃ COOH) of 2-(3-(benzyloxy)prop-1-yn-1-yl)-2,5,5-triethyl-3,4-bis(hydroxymethyl)pyrrolidin-1-oxyl (2e).....	S15
Figure S3. ¹ H NMR (500 MHz, CD ₃ OD, Zn/CF ₃ COOH) of 2-(3-(dimethylamino)prop-1-yn-1-yl)-2,5,5-triethyl-3,4-bis(hydroxymethyl)pyrrolidin-1-oxyl (2f).....	S16
Figure S4. ¹ H NMR (300 MHz, CD ₃ OD, Zn/CF ₃ COOH) of 2,2,5-triethyl-5-ethynyl-3,4-bis(((methylsulfonyl)oxy)methyl)pyrrolidin-1-oxyl (3a)	S16
Figure S5. ¹ H NMR (300 MHz, CD ₃ OD, Zn/CF ₃ COOH) of 2,2,5-triethyl-3,4-bis(((methylsulfonyl)oxy)methyl)-5-(phenylethynyl)pyrrolidin-1-oxyl (3b).....	S17
Figure S6. ¹ H NMR (300 MHz, CD ₃ OD, Zn/CF ₃ COOH) of 2,2,5-triethyl-3,4-bis(((methylsulfonyl)oxy)methyl)-5-((trimethylsilyl)ethynyl)pyrrolidin-1-oxyl (3d)	S17
Figure S7. ¹ H NMR (300 MHz, CD ₃ OD, Zn/CF ₃ COOH) of 2-(3-(dimethylamino)prop-1-yn-1-yl)-2,5,5-triethyl-3,4-bis(((methylsulfonyl)oxy)methyl)pyrrolidin-1-oxyl (3e)	S18
Figure S8. ¹ H NMR (400 MHz, CD ₃ OD, Zn/CF ₃ COOH) of 2-(3-(dimethylamino)prop-1-yn-1-yl)-2,5,5-triethyl-3,4-bis(((methylsulfonyl)oxy)methyl)pyrrolidin-1-oxyl (3f).....	S18
Figure S9. ¹ H NMR (400 MHz, CD ₃ OD, Zn/CF ₃ COOH) of 3,4-bis(acetoxymethyl)-2,2,5-triethyl-5-ethynylpyrrolidin-1-oxyl (5).....	S19
Figure S10. ¹ H NMR (300 MHz, CD ₃ OD, Zn/CF ₃ COOH) of 2,2,5-triethyl-3,4-bis(hydroxymethyl)-5-(3-phenyl-1 <i>H</i> -pyrazol-5-yl)pyrrolidin-1-oxyl (9a).....	S19
Figure S11. ¹ H NMR (300 MHz, CD ₃ OD, Zn/CF ₃ COOH) of 3b,5,5-triethyl-6-(((methylsulfonyl)oxy)methyl)-2-phenyl-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2- <i>b</i>]pyrazol-4-oxyl (9b)	S20
Figure S12. ¹ H NMR (300 MHz, CD ₃ OD, Zn/CF ₃ COOH) of 3b,5,5-triethyl-6-(hydroxymethyl)-2-phenyl-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2- <i>b</i>]pyrazol-4-oxyl (9c)	S20
IR spectra	S21
Figure S13. IR (KBr) of 2,2,5-triethyl-3,4-bis(hydroxymethyl)-5-((trimethylsilyl)ethynyl)pyrrolidin-1-oxyl (2d).....	S21
Figure S14. IR (neat) of 2-(3-(benzyloxy)prop-1-yn-1-yl)-2,5,5-triethyl-3,4-bis(hydroxymethyl)pyrrolidin-1-oxyl (2e).....	S21
Figure S15. IR (neat) of 2-(3-(dimethylamino)prop-1-yn-1-yl)-2,5,5-triethyl-3,4-bis(hydroxymethyl)pyrrolidin-1-oxyl (2f).....	S22
Figure S16. IR (KBr) of 2,2,5-triethyl-5-ethynyl-3,4-bis(((methylsulfonyl)oxy)methyl)pyrrolidin-1-oxyl (3a)	S22

Figure S17.	IR (neat) of 2,2,5-triethyl-3,4-bis(((methylsulfonyl)oxy)methyl)-5-(phenylethynyl)pyrrolidin-1-oxyl (3b)	S22
Figure S18.	IR (neat) of 2,2,5-triethyl-3,4-bis(((methylsulfonyl)oxy)methyl)-5-(3-((methylsulfonyl)oxy)prop-1-yn-1-yl)pyrrolidin-1-oxyl (3c).....	S23
Figure S19.	IR (neat) of 2,2,5-triethyl-3,4-bis(((methylsulfonyl)oxy)methyl)-5-((trimethylsilyl)ethynyl)pyrrolidin-1-oxyl (3d)	S23
Figure S20.	IR (neat) of 2-(3-(benzyloxy)prop-1-yn-1-yl)-2,5,5-triethyl-3,4-bis(((methylsulfonyl)oxy)methyl)pyrrolidin-1-oxyl (3e)	S23
Figure S21.	IR (neat) of 2-(3-(dimethylamino)prop-1-yn-1-yl)-2,5,5-triethyl-3,4-bis(((methylsulfonyl)oxy)methyl)pyrrolidin-1-oxyl (3f).....	S24
Figure S22.	IR (KBr) of 6-(azidomethyl)-3b,5,5-triethyl-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2-c][1,2,3]triazol-4-oxyl (4a).....	S24
Figure S23.	IR (KBr) of 6-(azidomethyl)-3b,5,5-triethyl-3-phenyl-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2-c][1,2,3]triazol-4-oxyl (4b).....	S24
Figure S24.	IR (KBr) of 3,6-bis(azidomethyl)-3b,5,5-triethyl-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2-c][1,2,3]triazol-4-oxyl (4c)	S25
Figure S25.	IR (KBr) of 6-(azidomethyl)-3b,5,5-triethyl-3-(trimethylsilyl)-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2-c][1,2,3]triazol-4-oxyl (4d).....	S25
Figure S26.	IR (neat) of 6-(azidomethyl)-3-((benzyloxy)methyl)-3b,5,5-triethyl-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2-c][1,2,3]triazol-4-oxyl (4e)	S25
Figure S27.	IR (neat) of 6-(azidomethyl)-3-((dimethylamino)methyl)-3b,5,5-triethyl-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2-c][1,2,3]triazol-4-oxyl (4f). S26	
Figure S28.	IR (neat) of 3,4-bis(acetoxymethyl)-2,2,5-triethyl-5-ethynylpyrrolidin-1-oxyl (5) S26	
Figure S29.	IR (neat) of 3,4-bis(acetoxymethyl)-2,2,5-triethyl-5-(3-oxo-3-phenylprop-1-yn-1-yl)pyrrolidin-1-oxyl (6a).....	S26
Figure S30.	IR (neat) of 2,2,5-triethyl-3,4-bis(((methylsulfonyl)oxy)methyl)-5-(3-oxo-3-phenylprop-1-yn-1-yl)pyrrolidin-1-oxyl (6b)	S27
Figure S31.	IR (KBr) of (Z)-2,2,6a-triethyl-3-(hydroxymethyl)-6-(2-oxoethylidene)hexahydro-1H-furo[3,4-b]pyrrol-1-oxyl (8)	S27
Figure S32.	IR (neat) 2,2,5-triethyl-3,4-bis(hydroxymethyl)-5-(3-phenyl-1H-pyrazol-5-yl)pyrrolidin-1-oxyl (9a).....	S27
Figure S33.	IR (neat) 3b,5,5-triethyl-6-(((methylsulfonyl)oxy)methyl)-2-phenyl-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2-b]pyrazol-4-oxyl (9b)	S28
Figure S34.	IR (KBr) 3b,5,5-triethyl-6-(hydroxymethyl)-2-phenyl-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2-b]pyrazol-4-oxyl (9c).....	S28
EPR measurements.....		S29
X-ray crystallographic analysis.....		S37

Experimental procedures

All commercially available solvents and reagents were of highest quality and used without further purification. Nitrone **1** and nitroxides **2a–c** was prepared according to the literature protocols [1]. NMR spectra for nitroxides were recorded after reduction by the Zn/CF₃COOH system in CD₃OD as describe [S1,S2]. ¹H NMR spectra were recorded at 300, 400 or 500 MHz on Bruker Avance AV 300, AV 400 and DRX 500 spectrometers, as indicated next to each NMR analysis. ¹H chemical shifts (δ) were internally referenced to the residual solvent peak. The *J* values in ¹H NMR spectra are given in Hz. The IR spectra were acquired on a FTIR spectrometer in KBr or neat. The UV spectra were recorded in EtOH (10⁻⁴ M solutions). The progress of the reactions was monitored by TLC and carried out using UV light at 254 nm, 10% solution of phosphomolybdic acid in ethanol, and/or Dragendorff reagent as visualizing agents. Column chromatography was performed on silica gel 60 (70–230 mesh). HRMS were recorded on a double-focusing, high-resolution mass spectrometer equipped with a high-performance toroidal ESA and quadrupole time-of-flight mass spectrometer\

S1. Dobrynin, S. A.; Gulman, M. M.; Morozov, D. A.; Zhurko, I. F.; Taratayko, A. I.; Sotnikova, Y. S.; Glazachev, Y. I.; Gatilov, Y. V.; Kirilyuk, I. A. Synthesis of Sterically Shielded Nitroxides Using the Reaction of Nitrones with Alkynylmagnesium Bromides. *Molecules* **2022**, 27 (21), 7626–7626. <https://doi.org/10.3390/molecules27217626>.

S2. Dobrynin, S. A.; Usatov, M. S.; Zhurko, I. F.; Morozov, D. A.; Polienko, Y. F.; Glazachev, Y. I.; Parkhomenko, D. A.; Tyumentsev, M. A.; Gatilov, Y. V.; Chernyak, E. I.; Bagryanskaya, E. G.; Kirilyuk, I. A. A Simple Method of Synthesis of 3-Carboxy-2,2,5,5-Tetraethylpyrrolidine-1-Oxyl and Preparation of Reduction-Resistant Spin Labels and Probes of Pyrrolidine Series. *Molecules* **2021**, 26 (19), 5761–5761. <https://doi.org/10.3390/molecules26195761>.

General method of the synthesis nitroxides 2d,e via reaction of nitrone with alkynylmagnesium bromide

A solution of corresponding terminal alkyne (trimethylsilylacetylene or benzyl propargyl ether) (0.14 mol) in dry THF (30 mL) was added dropwise to a solution of EtMgBr (2 M in THF, 70 mL). The mixture was stirred at room temperature for 30 min. A solution of nitrone **1** (5 g, 13.4 mmol) in dry THF (50 mL) was added to reaction mixture, and stirred for 3 days at room temperature, monitored by TLC (SiO₂, MeOH:ethyl acetate = 1:9, UV light for visualization). Upon completion, reaction mixture was quenched with water (10–15 mL). The precipitate was washed with ether (4 × 15 mL), and the combined organic phase was evaporated under reduced pressure The residue was dissolved in a mixture of methanol (50 mL) and water (10 mL).

Pyridinium *p*-toluenesulfonate (2 g, 8 mmol) was then added. The mixture stirred in air for oxidation (8 h). The reaction was monitored by TLC (SiO₂, MeOH:ethyl acetate = 1:9, Dragendorff reagent for visualization). After deprotection and oxidation, the reaction mixture was basified with 10 mL of 1 M aqueous solution of Na₂CO₃, and the methanol was removed in vacuum. The aqueous layer was extracted with ether (3 × 15 mL), dried over (Na₂CO₃), and evaporated in vacuum. The residue was purified by column chromatography (SiO₂, mixture of hexane and ethyl acetate).

2,2,5-Triethyl-3,4-bis(hydroxymethyl)-5-((trimethylsilyl)ethynyl)pyrrolidin-1-oxyl

(2d)

Yield 2.9 g (64%), yellow crystals, m.p. 69-74 °C. IR (KBr) ν_{\max} (cm⁻¹): 3473 (O-H), 3363 (O-H), 2968 (C-H), 2941 (C-H), 2881 (C-H), (C-H). 2171 (C≡C), 1247 (Si-CH₃); Anal. Calcd for C₁₇H₃₂NO₃Si: C, 62.53; H, 9.88; N, 4.29; SiO₂, 18.40; found: C, 62.40; H, 9.98; N, 4.57. SiO₂, 18.45; HRMS (EI/DFS) m/z [M]⁺ Calcd. for C₁₇H₃₂NO₃²⁸Si: 326.2146; found: 326.2141; ¹H NMR (300 MHz, CD₃OD, Zn/CF₃COOH, δ (ppm)): 0.21 (s, 9H), 0.97 (t, $J_t=7.4$ Hz, 3H), 0.97 (t, $J_t=7.4$ Hz, 3H), 1.19 (t, $J_t=7.2$ Hz, 3H), 1.85 (dq, $J_d=-14.0$ Hz, $J_q=7.4$ Hz, 1H), 1.94 (dq, $J_d=-14.0$ Hz, $J_q=7.4$ Hz, 1H), 2.00 (dq, $J_d=-13.6$ Hz, $J_q=7.4$ Hz, 1H), 2.11 (dq, $J_d=-13.6$ Hz, $J_q=7.4$ Hz, 1H), 2.14 (dq, $J_d=-13.2$ Hz, $J_q=7.2$ Hz, 1H), 2.23 (dq, $J_d=-13.2$ Hz, $J_q=7.2$ Hz, 1H), 2.29 (dd, $J_{d1}=2.3$ Hz, $J_{d2}=2.3$ Hz, 1H), 3.29 (ddd, $J_{d1}=6.0$ Hz, $J_{d2}=4.2$ Hz, $J_{d3}=4.2$ Hz, 1H), 3.71 (d, $J_d=4.2$ Hz, 2H), 3.81 (dd, $J_{d1}=2.3$ Hz, $J_{d2}=-12.1$ Hz, 1H), 3.89 (dd, $J_{d1}=2.3$ Hz, $J_{d2}=-12.1$ Hz 1H).

2-(3-(Benzyloxy)prop-1-yn-1-yl)-2,5,5-triethyl-3,4-bis(hydroxymethyl)pyrrolidin-1-oxyl (2e)

Yield 3.3g (66%), yellow oil, IR (neat) ν_{\max} (cm⁻¹): 3375 (O-H), 3089 (=C-H), 3064 (=C-H), 3031 (=C-H), 2970 (C-H), 2939 (C-H), 2881 (C-H). Anal. Calcd for C₂₂H₃₂NO₄: C, 70.56; H, 8.61; N, 3.74; Found: C, 70.70; H, 8.84; N, 3.46. HRMS (EI/DFS) m/z [M]⁺ Calcd. for C₂₂H₃₂NO₄: 374.2326; found: 374.2324. ¹H NMR (300 MHz, CD₃OD, Zn/CF₃COOH, δ (ppm)): 0.96 (t, $J_t=7.5$ Hz, 3H), 0.99 (t, $J_t=7.4$ Hz, 3H), 1.21 (t, $J_t=7.1$ Hz, 3H), 1.89 (dq, $J_d=-14.7$ Hz, $J_q=7.5$ Hz, 1H), 1.97 (dq, $J_d=-14.2$ Hz, $J_q=7.1$ Hz, 1H), 2.03 (dq, $J_d=-14.2$ Hz, $J_q=7.2$ Hz, 1H), 2.10 (dq, $J_d=-14.0$ Hz, $J_q=7.4$ Hz, 1H), 2.13 (dq, $J_d=-14.0$ Hz, $J_q=7.4$ Hz, 1H), 2.28 (dq, $J_d=-14.7$ Hz, $J_q=7.5$ Hz, 1H), 2.28 (ddd, $J_{d1}=4.3$ Hz, $J_{d2}=4.7$ Hz, $J_{d3}=9.9$ Hz, 1H), 2.34 (ddd, $J_{d1}=5.8$ Hz, $J_{d2}=7.0$ Hz, $J_{d3}=9.9$ Hz, 1H), 3.72 (d, $J_d=4.7$ Hz, 2H), 3.85 (dd, $J_{d1}=5.8$ Hz, $J_{d2}=-11.5$ Hz, 1H), 3.90 (dd, $J_{d1}=7.0$ Hz, $J_{d2}=-11.5$ Hz, 1H), 4.33 (s, 2H), 4.62 (s, 2H); 7.30-7.40 (m, 5H).

2-(3-(Dimethylamino)prop-1-yn-1-yl)-2,5,5-triethyl-3,4-bis(hydroxymethyl)pyrrolidin-1-oxyl (2f)

Copper(II) acetate monohydrate (0.2 g, 1 mmol) was added to a mixture of nitroxide **2a** (4.0 g, 15.7 mmol), 20% aqueous solution of formaldehyde (9.3 g, 62 mmol), 33% aqueous solution of dimethylamine (6.4 g, 47 mmol) in THF (350 mL) and heated under reflux for 24 h. The reaction was monitored by TLC (SiO₂, MeOH:ethyl acetate = 1:9, UV light for visualization). After cooling, the mixture was diluted with water (100 mL), and the THF was removed under reduced pressure. The resulting aqueous suspension was extracted with EtOAc (4 × 50 mL). The combined organic extracts were washed with water (50 mL) and then back-extracted with a 1 M aqueous solution of monosodium phosphate (2 × 100 mL). The combined water extract was basified with Na₂CO₃ to pH > 11 and extracted with ethyl acetate. The organic phase was dried over Na₂CO₃, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO₂, hexane:ethyl acetate = 2:1).

Yield 4.67 g (95%), orange oil. IR (neat) ν_{\max} (cm⁻¹): 3367 (O-H), 2968 (C-H), 2937 (C-H), 2879 (C-H), 2780 (C-H), 1043 (C-O). HRMS (EI/DFS) m/z [M]⁺ Calcd. for C₁₇H₃₁N₂O₃: 311.2379; found: 311.2382. ¹H NMR (500 MHz, CD₃OD, Zn/CF₃COOH, δ (ppm)): 0.98 (t, $J_t=7.4$ Hz, 3H), 1.02 (t, $J_t=7.4$ Hz, 3H), 1.21 (t, $J_t=7.4$ Hz, 3H), 1.97 (dq, $J_d=-15.1$ Hz, $J_q=7.4$ Hz, 1H), 1.98 (dq, $J_d=-15.1$ Hz, $J_q=7.4$ Hz, 1H), 2.06 (dq, $J_d=-14.7$ Hz, $J_q=7.4$ Hz, 1H), 2.08 (dq, $J_d=-9.8$ Hz, $J_q=7.4$ Hz, 1H), 2.11 (dq, $J_d=-9.8$ Hz, $J_q=7.4$ Hz, 1H), 2.32 (dq, $J_d=-14.7$ Hz, $J_q=7.4$ Hz, 1H), 2.30 (ddd, $J_{d1}=4.8$ Hz, $J_{d2}=5.1$ Hz, $J_{d3}=9.6$ Hz, 1H), 2.46 (ddd, $J_{d1}=6.0$ Hz, $J_{d2}=6.9$ Hz, $J_{d3}=9.4$ Hz, 1H), 3.01 (s, 6H); 3.73 (d, $J_d=4.8$ Hz, 1H), 3.73 (d, $J_d=5.1$ Hz, 1H), 3.89 (d, $J_d=6.0$ Hz, 1H), 3.89 (d, $J_d=6.9$ Hz, 1H), 4.28 (s, 2H).

General method of mesylation of nitroxides

A mixture of corresponding nitroxide **2a-f*** (2 mmol), DIPEA (6 mmol), MsCl (5 mmol) and dry chloroform (50 mL) was heated under reflux for 30 min. The reaction was monitored by TLC (SiO₂, mixtures of hexane and ether, 10% solution of phosphomolybdic acid for visualization). The mixture was washed with hot water. The organic layer was dried over Na₂CO₃, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO₂, hexane: ethyl acetate).

* Note: For nitroxide **2c**, the amounts of reagents were adjusted: DIPEA (8.5 mmol) and MsCl (7.5 mmol) were used.

2,2,5-Triethyl-5-ethynyl-3,4-bis(((methylsulfonyl)oxy)methyl)pyrrolidin-1-oxyl (3a)

Yield (91%) from compound **2a**, yellow crystals, m.p. 72-76 °C. IR (KBr) ν_{\max} (cm⁻¹): 3272 (\equiv C-H), 3031 (C-H), 2972 (C-H), 2941 (C-H), 2881 (C-H), 2112 (C \equiv C), 1357 (S=O), 1174 (S=O). Anal. Calcd for C₁₆H₂₈NO₇S₂: C, 46.81; H, 6.87; N, 3.41; S, 15.62; found: C, 47.06; H, 6.73; N, 3.53; S, 15.57. HRMS (EI/DFS) m/z [M]⁺ Calcd for C₁₆H₂₈NO₇³²S₂: 410.1300; found: 410.1302. ¹H NMR (300 MHz, CD₃OD, Zn/CF₃COOH, δ (ppm)): 0.99 (t, $J_t=7.4$ Hz, 3H), 1.02 (t, $J_t=7.3$ Hz, 3H), 1.23 (t, $J_t=7.4$ Hz, 3H), 1.92 (dq, $J_d=-15.0$ Hz, $J_q=7.3$ Hz, 1H), 1.97 (dq, $J_d=-15.0$ Hz, $J_q=7.3$ Hz, 1H), 2.07 (dq, $J_d=-14.6$ Hz, $J_q=7.4$ Hz, 1H), 2.17 (dq, $J_d=-13.5$ Hz, $J_q=7.4$ Hz, 1H), 2.21 (dq, $J_d=-13.5$ Hz, $J_q=7.4$ Hz, 1H), 2.22 (dq, $J_d=-14.6$ Hz, $J_q=7.4$ Hz, 1H), 2.73 (ddd, $J_{d1}=3.7$ Hz, $J_{d2}=5.5$ Hz, $J_{d3}=10.8$ Hz, 1H), 2.75 (ddd, $J_{d1}=4.7$ Hz, $J_{d2}=7.2$ Hz, $J_{d3}=10.8$ Hz, 1H), 3.16 (s, 3H), 3.17 (s, 3H), 3.65 (s, 1H), 4.42 (dd, $J_{d1}=3.8$ Hz, $J_{d2}=-11.3$ Hz, 1H), 4.51 (dd, $J_{d1}=5.5$ Hz, $J_{d2}=-11.3$ Hz, 1H), 4.58 (dd, $J_{d1}=7.2$ Hz, $J_{d2}=-11.0$ Hz, 1H), 4.60 (dd, $J_{d1}=4.7$ Hz, $J_{d2}=-11.0$ Hz, 1H);

2,2,5-Triethyl-3,4-bis(((methylsulfonyl)oxy)methyl)-5-(phenylethynyl)pyrrolidin-1-oxyl (3b)

Yield (84%) from compound **2b**, yellow oil. IR (neat) ν_{\max} (cm⁻¹): 3024 (=C-H), 2974 (C-H), 2939 (C-H), 2883 (C-H), 1358 (S=O), 1176 (S=O). Anal. Calcd for C₂₂H₃₂NO₇S₂: C, 54.30; H, 6.63; N, 2.88; S, 13.18; Found: C, 53.97; H, 6.69; N, 2.80; S, 13.42. HRMS (EI/DFS) m/z [M]⁺ Calcd for C₂₂H₃₂NO₇³²S₂: 489.1615; found: 489.1609. ¹H NMR (300 MHz, CD₃OD, Zn/CF₃COOH, δ (ppm)): 1.00 (t, $J_t=7.3$ Hz, 3H), 1.05 (t, $J_t=7.1$ Hz, 3H), 1.30 (t, $J_t=7.3$ Hz, 3H), 1.99 (q, $J_q=7.3$ Hz, 2H), 2.18 (dq, $J_d=-14.1$ Hz, $J_q=7.3$ Hz, 1H), 2.26 (dq, $J_d=-14.1$ Hz, $J_q=7.1$ Hz, 1H), 2.28 (dq, $J_d=-14.1$ Hz, $J_q=7.1$ Hz, 1H), 2.31 (dq, $J_d=-14.5$ Hz, $J_q=7.3$ Hz, 1H), 2.82 (ddd, $J_{d1}=4.4$ Hz, $J_{d2}=5.7$ Hz, $J_{d3}=10.0$ Hz, 1H), 2.83 (ddd, $J_{d1}=4.3$ Hz, $J_{d2}=7.0$ Hz, $J_{d3}=10.0$ Hz, 1H), 3.09 (s, 3H), 3.14 (s, 3H), 4.45 (dd, $J_{d1}=4.4$ Hz, $J_{d2}=-11.1$ Hz, 1H), 4.54 (dd, $J_{d1}=5.7$ Hz, $J_{d2}=-11.1$ Hz, 1H), 4.64 (dd, $J_{d1}=4.3$ Hz, $J_{d2}=-10.7$ Hz, 1H), 4.67 (dd, $J_{d1}=7.0$ Hz, $J_{d2}=-10.7$ Hz, 1H), 7.36 (dddd, $J_{d1}=0.8$ Hz, $J_{d2}=1.6$ Hz, $J_{d3}=7.6$ Hz, $J_{d4}=7.7$ Hz, 1H), 7.36 (dddd, $J_{d1}=0.8$ Hz, $J_{d2}=1.6$ Hz, $J_{d3}=7.6$ Hz, $J_{d4}=7.7$ Hz, 1H), 7.41 (dddd, $J_{d1}=1.3$ Hz, $J_{d2}=1.3$ Hz, $J_{d3}=7.6$ Hz, $J_{d4}=7.6$ Hz, 1H), 7.52 (dddd, $J_{d1}=0.8$ Hz, $J_{d2}=1.3$ Hz, $J_{d3}=2.2$ Hz, $J_{d4}=7.7$ Hz, 1H), 7.52 (dddd, $J_{d1}=0.8$ Hz, $J_{d2}=1.3$ Hz, $J_{d3}=2.2$ Hz, $J_{d4}=7.7$ Hz, 1H).

2,2,5-Triethyl-3,4-bis(((methylsulfonyl)oxy)methyl)-5-(3-((methylsulfonyl)oxy)prop-1-yn-1-yl)pyrrolidin-1-oxyl (3c)

Yield (83%) from compound **2c**, yellow oil. IR (neat) ν_{\max} (cm⁻¹): 2976 (C-H), 2941 (C-H), 2885 (C-H), 1354 (S=O), 1176 (S=O). Anal. Calcd for C₁₈H₃₂NO₁₀S₃: C, 41.69; H, 6.22; N, 2.70; S, 18.54; found: C, 41.35; H, 6.34; N, 2.57; S, 18.63.

**2,2,5-Triethyl-3,4-bis(((methylsulfonyl)oxy)methyl)-5-
((trimethylsilyl)ethynyl)pyrrolidin-1-oxyl (3d)**

Yield (91%) from compound **2d**, yellow oil. IR (neat) ν_{\max} (cm^{-1}): 2970 (C-H), 2941 (C-H), 2902 (C-H), 2885 (C-H), 2165 (C \equiv C), 1357 (S=O), 1178 (S=O). Anal. Calcd for $\text{C}_{19}\text{H}_{36}\text{NO}_7\text{S}_2\text{Si}$: C, 47.28; H, 7.52; N, 2.90; S, 13.29; Found: C, 47.52; H, 7.50; N, 3.05; S, 13.65. HRMS(EI/DFS) m/z $[\text{M}]^+$ Calcd for $\text{C}_{19}\text{H}_{36}\text{NO}_7^{32}\text{S}_2\text{Si}$: 482.1697, found: 482.1700. ^1H NMR (300 MHz, CD_3OD , $\text{Zn}/\text{CF}_3\text{COOH}$, δ (ppm)): 0.24 (s, 9H), 0.99 (t, $J_t=7.4$ Hz, 3H), 1.01 (t, $J_t=7.3$ Hz, 3H), 1.22 (t, $J_t=7.4$ Hz, 3H), 1.93 (dq, $J_d=-16.6$ Hz, $J_q=7.3$ Hz, 1H), 1.93 (dq, $J_d=-15.8$ Hz, $J_q=7.3$ Hz, 1H), 2.03 (dq, $J_d=-14.3$ Hz, $J_q=7.4$ Hz, 1H), 2.18 (dq, $J_d=-16.6$ Hz, $J_q=7.3$ Hz, 1H), 2.20 (dq, $J_d=-14.3$ Hz, $J_q=7.4$ Hz, 1H), 2.21 (dq, $J_d=-15.8$ Hz, $J_q=7.4$ Hz, 1H), 2.70 (ddd, $J_{d1}=4.1$ Hz, $J_{d2}=6.0$ Hz, $J_{d3}=10.9$ Hz, 1H), 2.71 (ddd, $J_{d1}=3.7$ Hz, $J_{d2}=7.8$ Hz, $J_{d3}=10.9$ Hz, 1H), 3.14 (s, 3H), 3.15 (s, 3H), 4.40 (dd, $J_{d1}=4.1$ Hz, $J_{d2}=-11.2$ Hz, 1H), 4.50 (dd, $J_{d1}=6.0$ Hz, $J_{d2}=-11.2$ Hz, 1H), 4.56 (dd, $J_{d1}=7.8$ Hz, $J_{d2}=-12.4$ Hz, 1H), 4.57 (dd, $J_{d1}=3.7$ Hz, $J_{d2}=-12.4$ Hz, 1H).

**2-(3-(Benzyloxy)prop-1-yn-1-yl)-2,5,5-triethyl-3,4-
bis(((methylsulfonyl)oxy)methyl)pyrrolidin-1-oxyl (3e)**

Yield (75%) from **2e**, yellow oil. IR (neat) ν_{\max} (cm^{-1}): 3027 (C-H), 2972 (C-H), 2939 (C-H), 2883 (C-H), 1358 (S=O), 1176 (S=O). Anal. Calcd for $\text{C}_{24}\text{H}_{36}\text{O}_8\text{NS}_2$: C, 54.32; H, 6.84; N, 2.64; S, 12.08, found: C, 54.52; H, 6.99; N, 2.78; S, 11.58. HRMS (EI/DFS) m/z $[\text{M}]^+$ Calcd for $\text{C}_{24}\text{H}_{36}\text{O}_8\text{N}^{32}\text{S}_2$: 530.1877; found: 530.1878. ^1H NMR (400 MHz, CD_3OD , $\text{Zn}/\text{CF}_3\text{COOH}$, δ (ppm)): 0.62 (t, $J_t=7.5$ Hz, 3H), 0.81 (t, $J_t=7.4$ Hz, 3H), 1.34 (t, $J_t=7.4$ Hz, 3H), 1.14-1.77 (m, 6H), 2.07-2.23 (m, 2H), 2.78 (s, 3H), 2.81 (s, 3H), 3.97 (s, 2H), 4.25 (s, 2H), 4.03 (dd, $J_{d1}=5.1$ Hz, $J_{d2}=-10.1$ Hz, 1H), 4.11 (dd, $J_{d1}=5.0$ Hz, $J_{d2}=-10.1$ Hz, 1H), 4.18 (dd, $J_{d1}=5.3$ Hz, $J_{d2}=-10.1$ Hz, 1H), 4.21 (dd, $J_{d1}=5.7$ Hz, $J_{d2}=-10.1$ Hz, 1H), 7.00-7.10 (m, 5H).

**2-(3-(Dimethylamino)prop-1-yn-1-yl)-2,5,5-triethyl-3,4-
bis(((methylsulfonyl)oxy)methyl)pyrrolidin-1-oxyl (3f)**

Yield (77%) from compound **2f**, yellow oil. IR (neat) ν_{\max} (cm^{-1}): 2974 (C-H), 2941 (C-H), 2988 (C-H), 2883 (C-H), 2825 (C-H), 2779 (C-H), 1356 (S=O), 1176 (S=O). Anal. Calcd for $\text{C}_{19}\text{H}_{35}\text{O}_7\text{NS}_2$: C, 48.80; H, 7.54; N, 5.99; S, 13.71, found: C, 49.22; H, 7.54; N, 5.77; S, 14.10. HRMS (EI/DFS) m/z $[\text{M}+1]^+$ Calcd for $\text{C}_{19}\text{H}_{36}\text{O}_7\text{N}^{32}\text{S}_2$: 468.1958; found: 468.1957. ^1H NMR (400 MHz, CD_3OD , $\text{Zn}/\text{CF}_3\text{COOH}$, δ (ppm)): 1.01 (t, $J_t=7.3$ Hz, 3H), 1.05 (t, $J_t=7.2$ Hz, 3H), 1.25 (t, $J_t=7.3$ Hz, 3H), 1.96 (dq, $J_d=-15.3$ Hz, $J_q=7.2$ Hz, 1H), 1.99 (dq, $J_d=-15.3$ Hz, $J_q=7.2$ Hz, 1H), 2.08 (dq, $J_d=-14.6$ Hz, $J_q=7.3$ Hz, 1H), 2.16 (dq, $J_d=-14.6$ Hz, $J_q=7.3$ Hz, 1H), 2.19 (dq, $J_d=-15.2$ Hz, $J_q=7.3$ Hz, 1H), 2.29 (dq, $J_d=-15.2$ Hz, $J_q=7.3$ Hz, 1H), 2.79 (ddd, $J_{d1}=4.7$ Hz, $J_{d2}=5.7$ Hz, $J_{d3}=10.8$ Hz, 1H), 2.81 (ddd, $J_{d1}=5.7$ Hz, $J_{d2}=6.5$ Hz, $J_{d3}=10.8$ Hz, 1H), 3.01 (s, 3H),

3.19 (s, 3H), 4.30 (d, $J_d=-16.4$ Hz, 1H), 4.32 (d, $J_d=-16.4$ Hz, 1H), 4.43 (dd, $J_{d1}=4.7$ Hz, $J_{d2}=-11.3$ Hz, 1H), 4.53 (dd, $J_{d1}=5.7$ Hz, $J_{d2}=-11.3$ Hz, 1H), 4.62 (dd, $J_{d1}=5.7$ Hz, $J_{d2}=-11.7$ Hz, 1H), 4.64 (dd, $J_{d1}=6.4$ Hz, $J_{d2}=-11.7$ Hz, 1H).

General method for the synthesis of tricyclic fused triazole derivatives

A mixture of corresponding nitroxide **3a-f*** (1mmol), sodium azide (4 mmol) and DMSO (10 mL) was stirred at 60 °C for 8 hours. The reaction was monitored by TLC (SiO₂, hexane:ethyl acetate mixtures, UV light for visualization). After cooling to room temperature, the mixture was diluted with water (50 mL) and extracted with ether (3 × 20 mL). The combined organic phase was evaporated under reduced pressure. The residue was purified by column chromatography (SiO₂, hexane:ethyl acetate mixtures).

* Note: For nitroxide **3c** 6 mmol of sodium azide was used.

6-(Azidomethyl)-3b,5,5-triethyl-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2-c][1,2,3]triazol-4-oxyl (4a)

Yield (97%) from compound **3a**, yellow crystals, m.p. 126-128 °C. IR(KBr) ν_{\max} (cm⁻¹): 2966 (C-H), 2879 (C-H), 2102 (N≡N). Anal. Calcd for C₁₄H₂₂N₇O: C, 55.25; H, 7.29; N, 32.21; found: C, 55.17; H, 7.29; N, 32.57. HRMS (EI/DFS) m/z [M]⁺ Calcd for C₁₄H₂₂N₇O: 304.1880; found: 304.1884.

6-(Azidomethyl)-3b,5,5-triethyl-3-phenyl-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2-c][1,2,3]triazol-4-oxyl (4b)

Yield (62%) from compound **3b**, yellow crystals, m.p. 108-109 °C. IR(KBr) ν_{\max} (cm⁻¹): 3063 (=C-H), 3034 (=C-H), 2983 (C-H), 2980 (C-H), 2937 (C-H), 2879 (C-H), 2112 (N≡N). Anal. Calcd for C₂₀H₂₆N₇O: C, 63.14; H, 6.89; N, 25.77; found: C, 63.03; H, 6.87; N, 25.78. HRMS (EI/DFS) m/z [M]⁺ Calcd for C₂₀H₂₆N₇O: 380.2193; found: 380.2190.

3,6-Bis(azidomethyl)-3b,5,5-triethyl-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2-c][1,2,3]triazol-4-oxyl (4c)

Yield (65%) from compound **3c**, yellow crystals, m.p. 85-86 °C. IR(KBr) ν_{\max} (cm⁻¹): 2976 (C-H), 2964 (C-H), 2937 (C-H), 2924 (C-H), 2881 (C-H), 2116 (N=N=N), 2081 (N=N=N). Anal. Calcd for C₁₅H₂₃N₁₀O: C, 50.13; H, 6.45; N, 38.97; found: C, 50.38; H, 6.44; N, 38.95. HRMS(EI/DFS) m/z [M]⁺ Calcd for C₁₅H₂₃N₁₀O: 359.2051; found: 359.2045.

6-(Azidomethyl)-3b,5,5-triethyl-3-(trimethylsilyl)-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2-c][1,2,3]triazol-4-oxyl (4d)

Yield (45%) from **3d**, yellow crystals, m.p. 65-70 °C. IR(KBr) ν_{\max} (cm⁻¹): 2968 (C-H), 2935 (C-H), 2877 (C-H), 2104 (N≡N). Anal. Calcd for C₁₇H₃₀N₇OSi: C, 54.22; H, 8.03; N, 26.04; found: C, 53.88; H, 8.08; N, 26.30. HRMS (EI/DFS) m/z [M]⁺ Calcd for C₁₇H₃₀N₇OSi: 376.2276; found: 376.2271.

6-(Azidomethyl)-3-((benzyloxy)methyl)-3b,5,5-triethyl-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2-c][1,2,3]triazol-4-oxyl (4e)

Yield (65%) from **3e**. yellow oil. IR(neat) ν_{\max} (cm⁻¹): 3087 (=C-H), 3064 (=C-H), 3032 (=C-H), 2972 (C-H), 2937 (C-H), 2937 (C-H), 2881 (C-H), 2102 (N≡N). Anal. Calcd for C₂₂H₃₀N₇O₂: C, 62.24; H, 7.12; N, 23.10; found: C, 62.03; H, 6.87; N, 22.78. HRMS (EI/DFS) m/z [M]⁺ Calcd for C₂₂H₃₀N₇O₂: 424.2456; found : 424.2446.

6-(Azidomethyl)-3-((dimethylamino)methyl)-3b,5,5-triethyl-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2-c][1,2,3]triazol-4-oxyl (4f)

Yield (66%) from compound **3f**. yellow oil. IR(neat) ν_{\max} (cm⁻¹): 2972 (C-H), 2939 (C-H), 2881 (C-H), 2823 (C-H), 2777 (C-H), 2100 (N≡N). Anal. Calcd for C₁₇H₂₉N₈O: C, 56.49; H, 8.09; N, 31.00. found: C, 56.49; H, 8.06; N, 30.82. HRMS (EI/DFS) m/z [M]⁺ Calcd for C₁₇H₂₉N₈O: 361.2459; found: 361.2456.

3,4-Bis(acetoxymethyl)-2,2,5-triethyl-5-ethynylpyrrolidin-1-oxyl (5)

A mixture of nitroxide **2a** (1.5 g, 6 mmol), acetic anhydride (15 mL, 150 mmol), and sodium acetate (2.0 g, 25 mmol) in chloroform (15 mL) was stirred for 24 hours at room temperature. The reaction progress was monitored by TLC (SiO₂, hexane/ethyl acetate = 1:1, UV light for visualization). The precipitate was removed by filtration, and the filtrate was concentrated under reduced pressure. The residue was separated using column chromatography (SiO₂, hexane:ethyl acetate = 1:1) to afford the product as a yellow oil 1.7 g (84%). IR (neat) ν_{\max} (cm⁻¹): 3259 (≡C-H), 2972 (C-H), 2939 (C-H), 2883 (C-H), 2107 (C≡C), 1743 (C=O), 1241 (C(O)-O), 1039 (C-O). Anal. Calcd. for C₁₈H₂₈O₅N: C, 63.88; H, 8.34; N, 4.14; found: C, 63.94; H, 8.40; N, 4.15; HRMS (EI/DFS) m/z [M]⁺ Calcd. for C₁₈H₂₈O₅N: 338.1962; found: 338.1961; ¹H NMR (300 MHz, CD₃OD, Zn/CF₃COOH, δ) 0.98 (t, *J*_t=7.3 Hz, 3H), 1.01 (t, *J*_t=7.2 Hz, 3H), 1.23 (t, *J*_t=7.3 Hz, 3H); 1.90 (q, *J*_q=7.3 Hz, 2H), 2.06 (q, *J*_q=7.3 Hz, 2H), 2.19 (q, *J*_q=7.2 Hz, 2H); 2.05 (s, 3H), 2.07 (s, 3H); 2.53 (ddd, *J*_{d1}=4.7 Hz, *J*_{d2}=7.0 Hz, *J*_{d3}=11.4 Hz, 1H), 2.62 (ddd, *J*_{d1}=4.1 Hz, *J*_{d2}=6.4 Hz, *J*_{d3}=11.4 Hz, 1H); 3.48 (s, 1H); 4.26 (dd, *J*_{d1}=4.1 Hz, *J*_{d2}=-12.2 Hz, 1H),

4.32 (dd, $J_{d1}=6.4$ Hz, $J_{d2}=-12.2$ Hz, 1H), 4.34 (dd, $J_d=7.0$ Hz, $J_{d2}=-11.9$ Hz, 1H), 4.48 (dd, $J_{d1}=4.7$ Hz, $J_{d2}=-11.9$ Hz, 1H).

General method for the synthesis of alkynones

The reaction was performed under an argon atmosphere. To a stirred mixture of terminal alkyne (**5** or **3a**) (0.6 mmol), Pd(PPh₃)₂Cl₂ (17 mg, 0.024 mmol), CuI (5 mg, 0.024 mmol), PPh₃ (6 mg, 0.024 mmol), and NEt₃ (182 mg, 1.8 mmol) in toluene (15 mL) was added benzoyl chloride (168 mg, 1.2 mmol). The solution was heated under reflux for 4 hours, and monitored by TLC (SiO₂, hexane/ethyl acetate = 3:1, UV light for visualization). The solvent was evaporated under reduced pressure, and the residue was taken up in diethyl ether. The precipitate was removed by filtration, and the filtrate was concentrated under reduced pressure. The crude product was separated using column chromatography (SiO₂, hexane:ethyl acetate = 2:1, UV light for visualization) to afford the title compound.

3,4-Bis(acetoxymethyl)-2,2,5-triethyl-5-(3-oxo-3-phenylprop-1-yn-1-yl)pyrrolidin-1-oxyl (**6a**)

Yield 230 mg, (89%) from **5**. IR (neat) ν_{max} (cm⁻¹): 3026 (=C-H), 2974 (C-H), 2939 (C-H), 2883 (C-H), 2214 (C≡C), 1645 (C=O), 1265 (C(O)-O), 1358, 1176, 958, 831(C-O); Anal. Calcd. for C₂₅H₃₂O₆N: C, 67.85; H, 7.29; N, 3.17 found: C, 67.42; H, 7.17; N, 3.25; HRMS (EI/DFS) m/z [M]⁺ Calcd. for C₂₅H₃₂O₆N: 442.2224; found: 442.2223.

3,4-Bis(((methylsulfonyl)oxy)methyl)-2,2,5-triethyl-5-(3-oxo-3-phenylprop-1-yn-1-yl)pyrrolidin-1-oxyl (**6b**)

Yield 136 mg (44%) from compound **3a**. yellow oil. IR (neat) ν_{max} (cm⁻¹): 3064 (=C-H), 2974 (C-H), 2939 (C-H), 2883 (C-H), 2212 (C≡C), 1745 (C=O), 1647 (C=O), 1243 (C(O)-O), 1041 (C-O); HRMS (EI/DFS) m/z [M]⁺ Calcd. for C₂₃H₃₂O₈N³²S₂: 514.1564; found: 514.1560.

2,2,6a-Triethyl-3-(hydroxymethyl)-1-6-(2-oxoethylidene)hexahydro-1H-furo[3,4-b]pyrrol-1-oxyl (**8**)

To a solution of compound **2c** (0.5 g, 2 mmol) in tetrahydrofuran was added manganese(IV) oxide (MnO₂, 5 g, 60 mmol). The reaction mixture was stirred at room temperature for 3 days and monitored by monitored by TLC (SiO₂, ethyl acetate). Upon completion of the reaction, the solid was removed by filtration, and the filtrate was concentrated under reduced pressure. The residue was triturated with ether and the product was collected 0.28 g (50% yield) as yellow crystals, m.p. 100–103 °C. IR (KBr) ν_{max} (cm⁻¹): 3387 (O-H), 2976 (C-H), 2939 (C-H), 2908 (C-H), 2881 (C-H), 2864 (C-H) 1639 (C=O), 1614 (C=C), 1157 (C-O);

Anal. Calcd for C₁₅H₂₄O₄N: C, 63.81; H, 8.57; N, 4.96; found: C, 63.68; H, 8.39; N, 4.92; HRMS (EI/DFS) m/z [M]⁺ Calcd for C₁₅H₂₄O₄N: 282.3629; found: 282.3625.

2,2,5-Triethyl-3,4-bis(hydroxymethyl)-5-(3-phenyl-1*H*-pyrazol-5-yl)pyrrolidin-1-oxyl (9a)

The mixture of nitroxide **6a** (200 mg, 0.5 mmol) and hydrazine hydrate (600 mg, 12.0 mmol) in diethyl ether (50 mL) was stirred vigorously at room temperature for 3 days and monitored by TLC (SiO₂, hexane/EtOAc, 1:1, UV light for visualization). The mixture was washed with 1 M aqueous solution of monosodium phosphate (3 × 15 mL). The organic layer was dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was dissolved in methanol (20 mL), and a 2.5 M aqueous NaOH solution (10 mL) was added. After stirring for 2 days, the mixture was diluted with water (50 mL). Methanol was removed in vacuo, and the aqueous layer was extracted with ethyl acetate (3 × 15 mL). The combined organic extracts were dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was triturated with ether and the product 57 mg (33%) was collected as yellow crystals. m.p. 184–186 °C. IR (KBr) ν_{max} (cm⁻¹): 3240 (O-H), 3130 (O-H), 3070 (=C-H), 3053 (=C-H), 3037 (=C-H), 3018 (=C-H), 2966 (C-H), 2939 (C-H), 2881 (C-H); Anal. Calcd. for C₂₁H₃₀O₃N₃: C, 67.71; H, 8.12; N, 11.28; found: C, 67.75; H, 8.28; N, 11.26; HRMS (EI/DFS) m/z [M]⁺ Calcd. for C₂₁H₃₀O₃N₃: 372.2282; found: 372.2280; ¹H NMR (300 MHz, CD₃OD, Zn/CF₃COOH, δ): 0.98 (t, *J*_t=7.3 Hz, 3H), 1.12 (t, *J*_t=7.5 Hz, 3H), 1.13 (t, *J*_t=7.3 Hz, 3H); 1.94 (dq, *J*_d=-15.7 Hz, *J*_q=7.3 Hz, 1H), 2.00 (dq, *J*_d=-15.7 Hz, *J*_q=7.3 Hz, 1H), 2.16 (dq, *J*_d=-14.3 Hz, *J*_q=7.5 Hz, 1H), 2.22 (dq, *J*_d=-9.2 Hz, *J*_q=7.3 Hz, 1H), 2.35 (dq, *J*_d=-14.3 Hz, *J*_q=7.5 Hz, 1H), 2.57 (dq, *J*_d=-9.2 Hz, *J*_q=7.3 Hz, 1H), 2.63; 2.22 (ddd, *J*_{d1}=6.5 Hz, *J*_{d2}=7.0 Hz, *J*_{d3}=11.9 Hz, 1H), 2.63 (ddd, *J*_{d1}=5.1 Hz, *J*_{d2}=6.3 Hz, *J*_{d3}=11.9 Hz, 1H); 3.61 (dd, *J*_{d1}=7.0 Hz, *J*_{d2}=-11.4 Hz, 1H), 3.70 (dd, *J*_{d1}=6.5 Hz, *J*_{d2}=-11.4 Hz, 1H), 3.73 (dd, *J*_{d1}=6.3 Hz, *J*_{d2}=-11.6 Hz, 1H), 3.80 (dd, *J*_{d1}=5.1 Hz, *J*_{d2}=-11.6 Hz, 1H); 6.73 (s, 1H); 7.39 (dddd, *J*_{d1}=1.2 Hz, *J*_{d2}=1.2 Hz, *J*_{d3}=7.4 Hz, *J*_{d4}=7.4 Hz, 1H), 7.47 (dddd, *J*_{d1}=0.6 Hz, *J*_{d2}=1.0 Hz, *J*_{d3}=7.5 Hz, *J*_{d4}=7.8 Hz, 1H), 7.47 (dddd, *J*_{d1}=0.6 Hz, *J*_{d2}=1.0 Hz, *J*_{d3}=7.4 Hz, *J*_{d4}=7.8 Hz, 1H), 7.72 (dddd, *J*_{d1}=0.6 Hz, *J*_{d2}=1.2 Hz, *J*_{d3}=1.7 Hz, *J*_{d4}=7.8 Hz, 1H), 7.72 (dddd, *J*_{d1}=0.6 Hz, *J*_{d2}=1.2 Hz, *J*_{d3}=1.7 Hz, *J*_{d4}=7.8 Hz, 1H).

Annulated tricyclic pyrazole derivatives synthesis

Method A: A mixture of nitroxide **9a** (2.0 g, 5.4 mmol), *N,N*-diisopropylethylamine (2.1 g, 16.0 mmol) and methanesulfonyl chloride (2.3 g, 16.0 mmol) in dry CHCl₃ (50 mL) was heated under reflux for 30 min. The reaction was monitored by TLC (SiO₂, hexane:diethyl ether

1:1, UV light for visualization). The mixture was washed with hot water (60 °C, 3 × 50 mL). The organic phase was evaporated under reduced pressure, and the crude residue was purified by column chromatography (SiO₂ hexane:diethyl ether = 1:4) to afford the two products **9b** (1.0 g, 43%) and **9c** (0.5 g, 26%).

Method B: A mixture of nitroxide **9a** (2.0 g, 5.4 mmol), *N,N*-diisopropylethylamine (4.2 g, 32.0 mmol) and methanesulfonyl chloride (3.9 g, 27.0 mmol) in dry CHCl₃ (50 mL) was heated under reflux for 30 min. The reaction was monitored by TLC (SiO₂, hexane:diethyl ether 1:1, UV light for visualization). The mixture was washed with hot water (60 °C, 3 × 50 mL). The organic phase was evaporated under reduced pressure, and the crude residue was purified by column chromatography (SiO₂ hexane:diethyl ether = 1:4) to afford 1.5 g (65%) of nitroxide **9b**.

Method C.

The mixture nitroxide **6b** (200 mg, 0.4 mmol) and hydrazine hydrate (250 mg, 5.0 mmol) in diethyl ether (10 mL) was stirred vigorously at room temperature for 1 day and monitored by TLC (SiO₂, hexane/ether, 1:4, UV light for visualization). The mixture was washed with 1 M aqueous solution of monosodium phosphate (3 × 5 mL). The organic layer was dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was dissolved in methanol (20 mL) and stirred under an ambient atmosphere for 24 hours to oxidation. The solvent was evaporated under reduced pressure, and the crude residue was purified by column chromatography (SiO₂, hexane:diethyl ether = 1:4) to afford the product as an oily substance **9b** (73 mg, 42%).

3b,5,5-Triethyl-6-(((methylsulfonyl)oxy)methyl)-2-phenyl-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2-*b*]pyrazol-4-oxyl (9b**)**

Yellow oil. IR (neat) ν_{\max} (cm⁻¹): 3135 (=C-H), 3018 (=C-H), 2976 (C-H), 2939 (C-H), 2883 (C-H), 1352 (S=O), 1176 (S=O); HRMS (EI/DFS) *m/z* [M]⁺ Calcd for C₂₂H₃₀O₄N₃³²S: 432.1952; found: 432.1953; ¹H NMR (300 MHz, CD₃OD, Zn/CF₃COOH, δ) 0.91 (t, *J*_t=7.3 Hz, 3H), 0.95 (t, *J*_t=7.3 Hz, 3H), 1.09 (t, *J*_t=7.3 Hz, 3H); 1.23 (dq, *J*_d=-14.5 Hz, *J*_q=7.3 Hz, 1H), 1.68 (dq, *J*_d=-14.5 Hz, *J*_q=7.3 Hz, 1H), 1.98 (dq, *J*_d=-15.3 Hz, *J*_q=7.3 Hz, 1H), 2.03 (dq, *J*_d=-15.3 Hz, *J*_q=7.3 Hz, 1H), 2.20 (dq, *J*_d=-13.7 Hz, *J*_q=7.3 Hz, 1H), 2.36 (dq, *J*_d=-13.7 Hz, *J*_q=7.3 Hz, 1H); 2.81 (ddd, *J*_d=5.8 Hz, *J*_d=5.3 Hz, *J*_d=4.9 Hz, 1H), 3.65 (ddd, *J*_d=7.7 Hz, *J*_d=5.8 Hz, *J*_d=1.9 Hz, 1H); 3.23 (s, 3H); 4.40 (dd, *J*_{d1}=-11.9 Hz, *J*_{d2}=1.9 Hz, 1H), 4.51 (dd, *J*_{d1}=-10.8 Hz, *J*_{d2}=4.9 Hz, 1H), 4.58 (dd, *J*_{d1}=-10.8 Hz, *J*_{d2}=5.3 Hz, 1H), 4.60 (dd, *J*_{d1}=-11.9 Hz, *J*_{d2}=7.7 Hz, 1H); 6.80 (s, 1H); 7.35 (dddd, *J*_{d1}=7.1 Hz, *J*_{d2}=7.4 Hz, *J*_{d3}=1.1 Hz, *J*_{d4}=1.1 Hz, 1H), 7.42 (dddd, *J*_{d1}=7.8 Hz, *J*_{d2}=7.4 Hz, *J*_{d3}=1.1 Hz, *J*_{d4}=0.7

Hz, 1H), 7.80 (dddd, $J_{d1}=7.8$ Hz, $J_{d2}=1.7$ Hz, $J_{d3}=1.1$ Hz, $J_{d4}=0.6$ Hz, 1H), 7.80 (dddd, $J_{d1}=7.8$ Hz, $J_{d2}=1.7$ Hz, $J_{d3}=1.1$ Hz, $J_{d4}=0.6$ Hz, 1H).

3b,5,5-Triethyl-6-(hydroxymethyl)-2-phenyl-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2-*b*]pyrazol-4-oxyl (9c)

Yellow crystals, m.p. 56-59 °C. IR (KBr) ν_{\max} (cm⁻¹): 3356 (O-H), 3062 (=C-H), 3037 (=C-H), 2970 (C-H), 2937 (C-H), 2881 (C-H); HRMS (EI/DFS) m/z [M]⁺ Calcd for C₂₁H₂₈O₂N₃: 354.2176; found: 354.2171; ¹H NMR (300 MHz, CD₃OD, Zn/CF₃COOH, δ) 0.87 (t, $J_t=7.3$ Hz, 3H), 0.94 (t, $J_t=7.3$ Hz, 3H), 1.05 (t, $J_t=7.3$ Hz, 3H); 1.18 (dq, $J_d=-14.4$ Hz, $J_q=7.3$ Hz, 1H), 1.49 (dq, $J_d=-14.4$ Hz, $J_q=7.3$ Hz, 1H), 2.00 (dq, $J_d=-15.1$ Hz, $J_q=7.3$ Hz, 1H), 2.10 (dq, $J_d=-15.1$ Hz, $J_q=7.3$ Hz, 1H), 2.27 (dq, $J_d=-13.5$ Hz, $J_q=7.3$ Hz, 1H), 2.34 (dq, $J_d=-13.5$ Hz, $J_q=7.3$ Hz, 1H); 2.49 (ddd, $J_d=3.5$ Hz, $J_d=3.5$ Hz, $J_d=3.7$ Hz, 1H), 3.65 (ddd, $J_d=2.5$ Hz, $J_d=3.7$ Hz, $J_d=8.8$ Hz, 1H); 3.81 (dd, $J_{d1}=-10.8$ Hz, $J_{d2}=3.5$ Hz, 1H), 3.88 (dd, $J_{d1}=-10.8$ Hz, $J_{d2}=3.5$ Hz, 1H), 4.33 (dd, $J_{d1}=-12.1$ Hz, $J_{d2}=2.5$ Hz, 1H), 4.62 (dd, $J_{d1}=-12.1$ Hz, $J_{d2}=8.7$ Hz, 1H); 6.75 (s, 1H); 7.34 (dddd, $J_{d1}=7.1=4$ Hz, $J_{d2}=7.4$ Hz, $J_{d3}=1.2$ Hz, $J_{d4}=1.2$ Hz, 1H), 7.42 (dddd, $J_{d1}=7.8$ Hz, $J_{d2}=7.4$ Hz, $J_{d3}=1.0$ Hz, $J_{d4}=0.6$ Hz, 1H), 7.42 (dddd, $J_{d1}=7.8$ Hz, $J_{d2}=7.4$ Hz, $J_{d3}=1.0$ Hz, $J_{d4}=0.6$ Hz, 1H), 7.80 (dddd, $J_{d1}=7.8$ Hz, $J_{d2}=1.8$ Hz, $J_{d3}=1.2$ Hz, $J_{d4}=0.6$ Hz, 1H), 7.80 (dddd, $J_{d1}=7.8$ Hz, $J_{d2}=1.8$ Hz, $J_{d3}=1.2$ Hz, $J_{d4}=0.6$ Hz, 1H).

NMR spectra

Figure S1. ^1H NMR (300 MHz, CD_3OD , $\text{Zn}/\text{CF}_3\text{COOH}$) of 2,2,5-triethyl-3,4-bis(hydroxymethyl)-5-((trimethylsilyl)ethynyl)pyrrolidin-1-oxyl (2d)

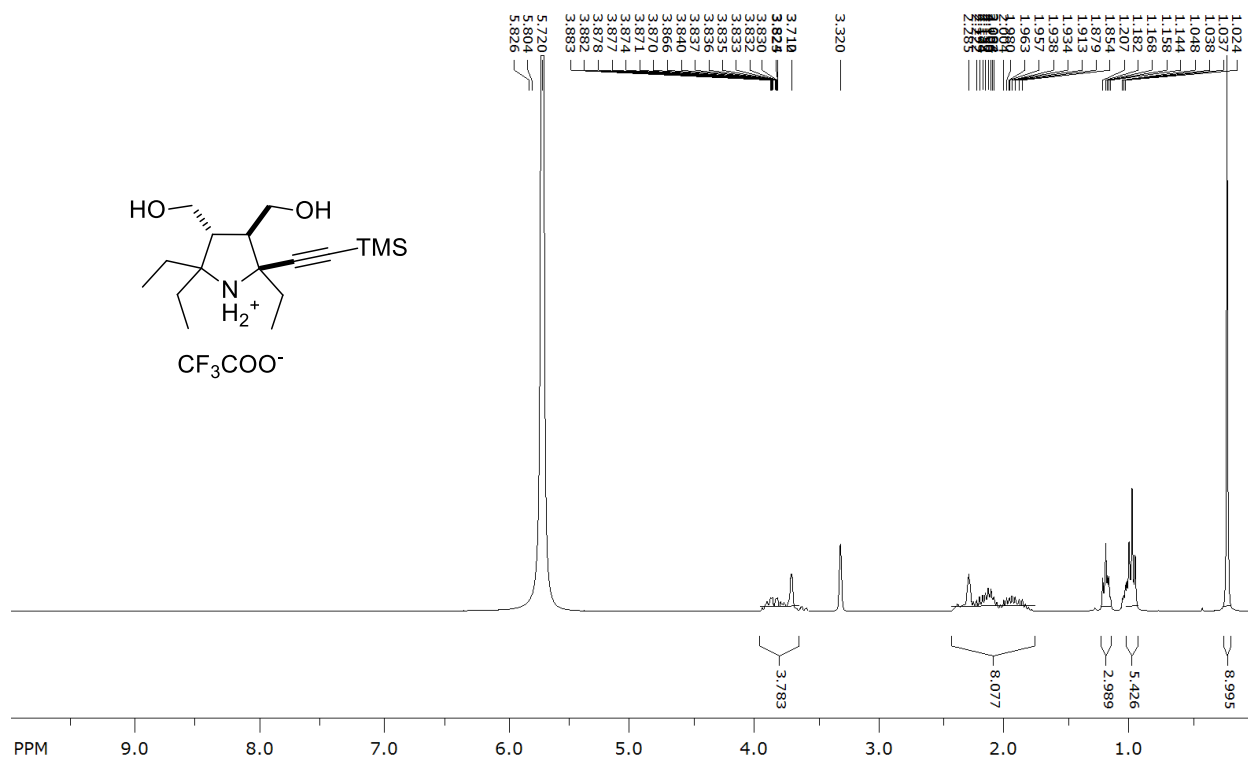


Figure S2. ^1H NMR (300 MHz, CD_3OD , $\text{Zn}/\text{CF}_3\text{COOH}$) of 2-(3-(benzyloxy)prop-1-yn-1-yl)-2,5,5-triethyl-3,4-bis(hydroxymethyl)pyrrolidin-1-oxyl (2e)

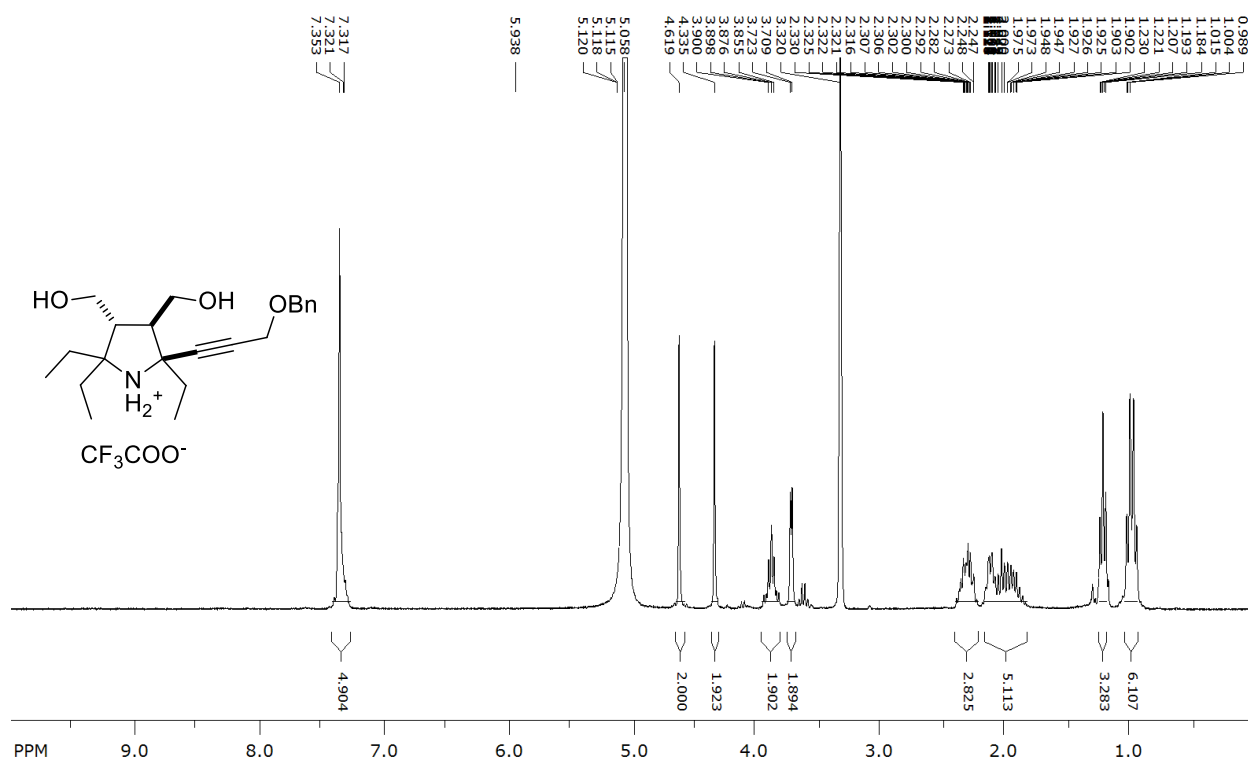


Figure S3. ^1H NMR (500 MHz, CD_3OD , $\text{Zn}/\text{CF}_3\text{COOH}$) of 2-(3-(dimethylamino)prop-1-yn-1-yl)-2,5,5-triethyl-3,4-bis(hydroxymethyl)pyrrolidin-1-oxyl (2f)

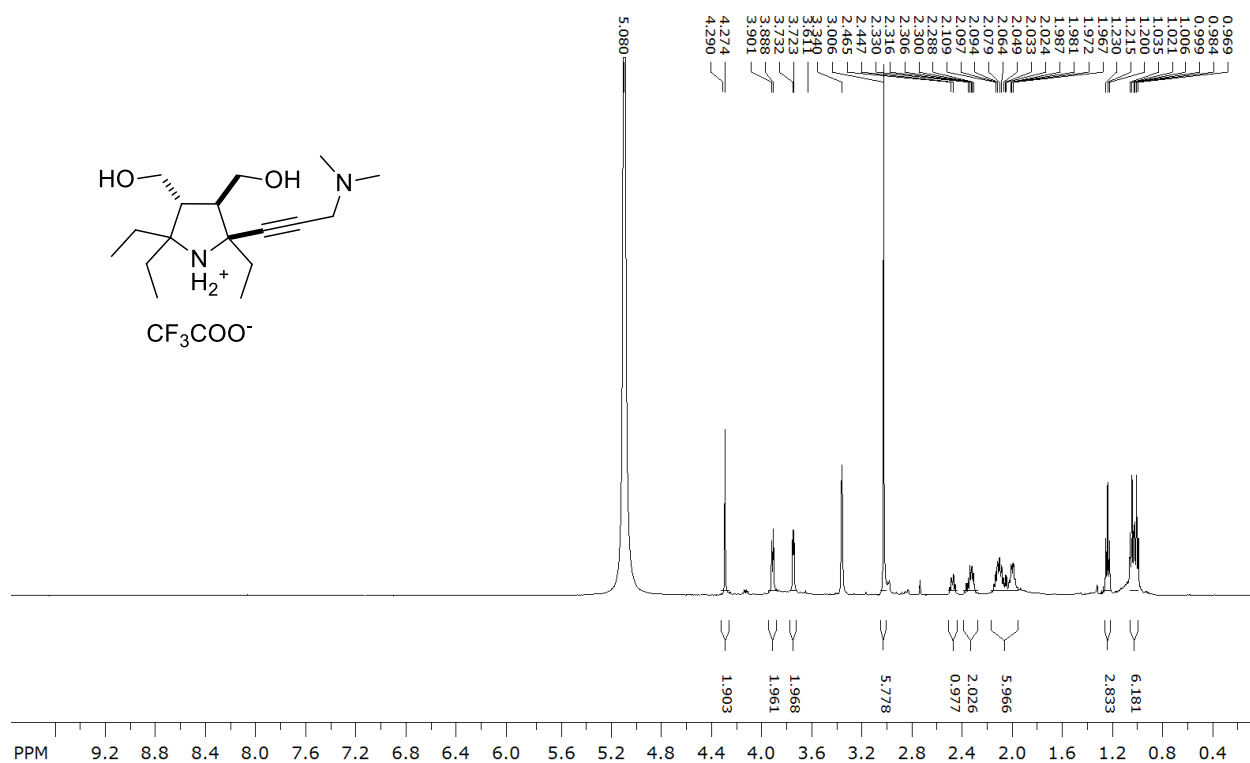


Figure S4. ^1H NMR (300 MHz, CD_3OD , $\text{Zn}/\text{CF}_3\text{COOH}$) of 2,2,5-triethyl-5-ethynyl-3,4-bis(((methylsulfonyl)oxy)methyl)pyrrolidin-1-oxyl (3a)

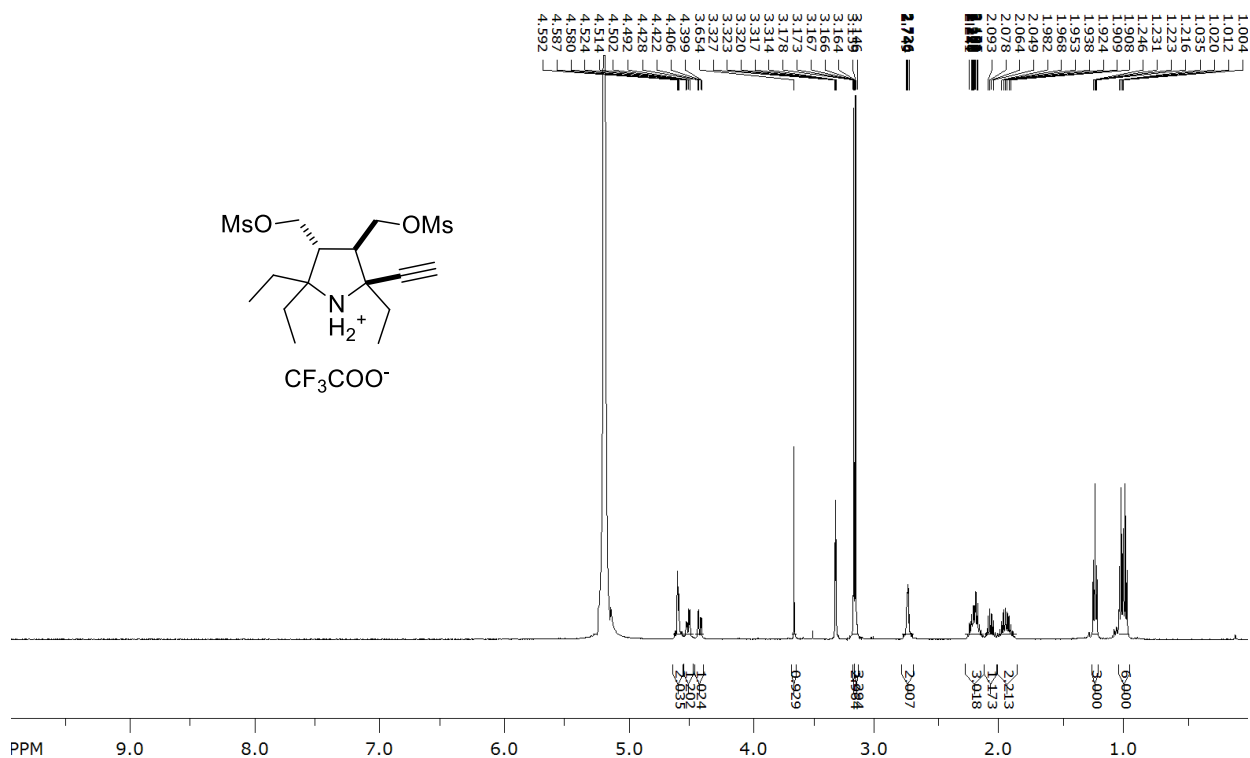


Figure S9. ^1H NMR (400 MHz, CD_3OD , $\text{Zn}/\text{CF}_3\text{COOH}$) of 3,4-bis(acetoxymethyl)-2,2,5-triethyl-5-ethynylpyrrolidin-1-oxyl (5)

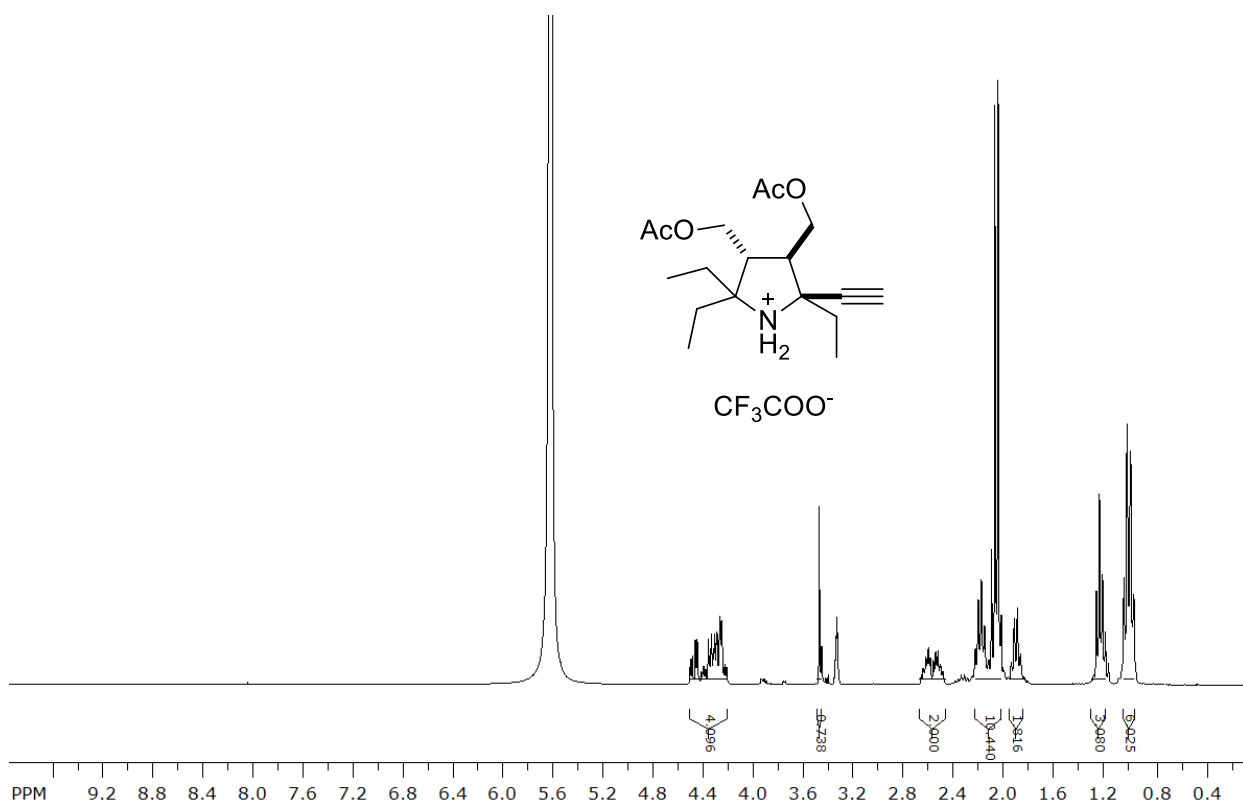


Figure S10. ^1H NMR (300 MHz, CD_3OD , $\text{Zn}/\text{CF}_3\text{COOH}$) of 2,2,5-triethyl-3,4-bis(hydroxymethyl)-5-(3-phenyl-1H-pyrazol-5-yl)pyrrolidin-1-oxyl (9a)

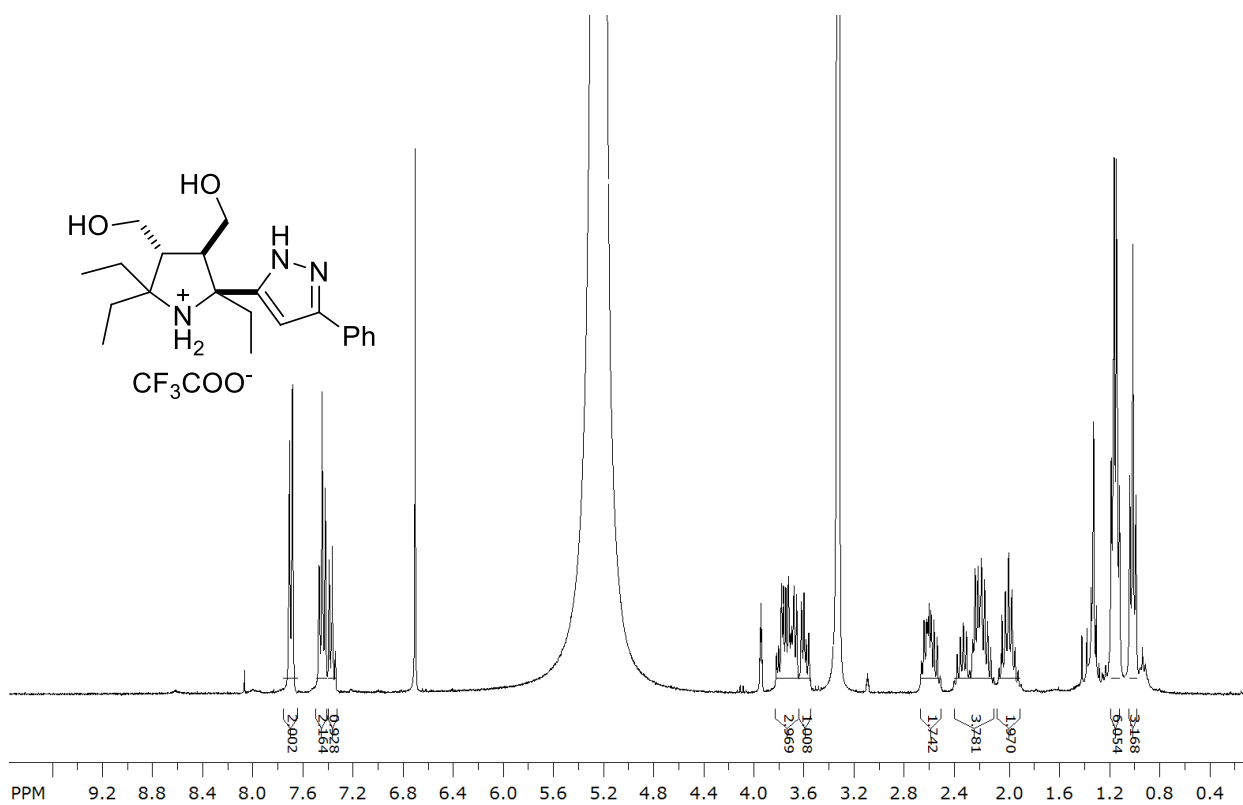


Figure S11. ^1H NMR (300 MHz, CD_3OD , $\text{Zn}/\text{CF}_3\text{COOH}$) of 3b,5,5-triethyl-6-(((methylsulfonyl)oxy)methyl)-2-phenyl-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2-*b*]pyrazol-4-oxyl (9b)

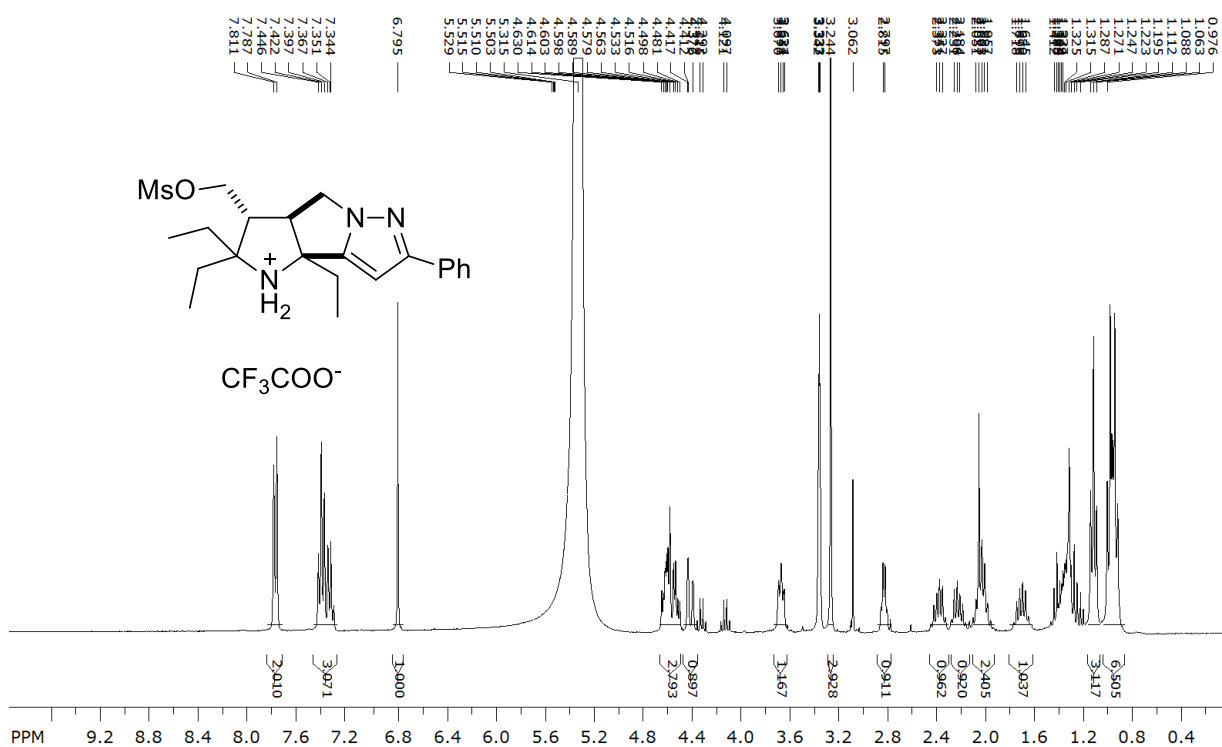
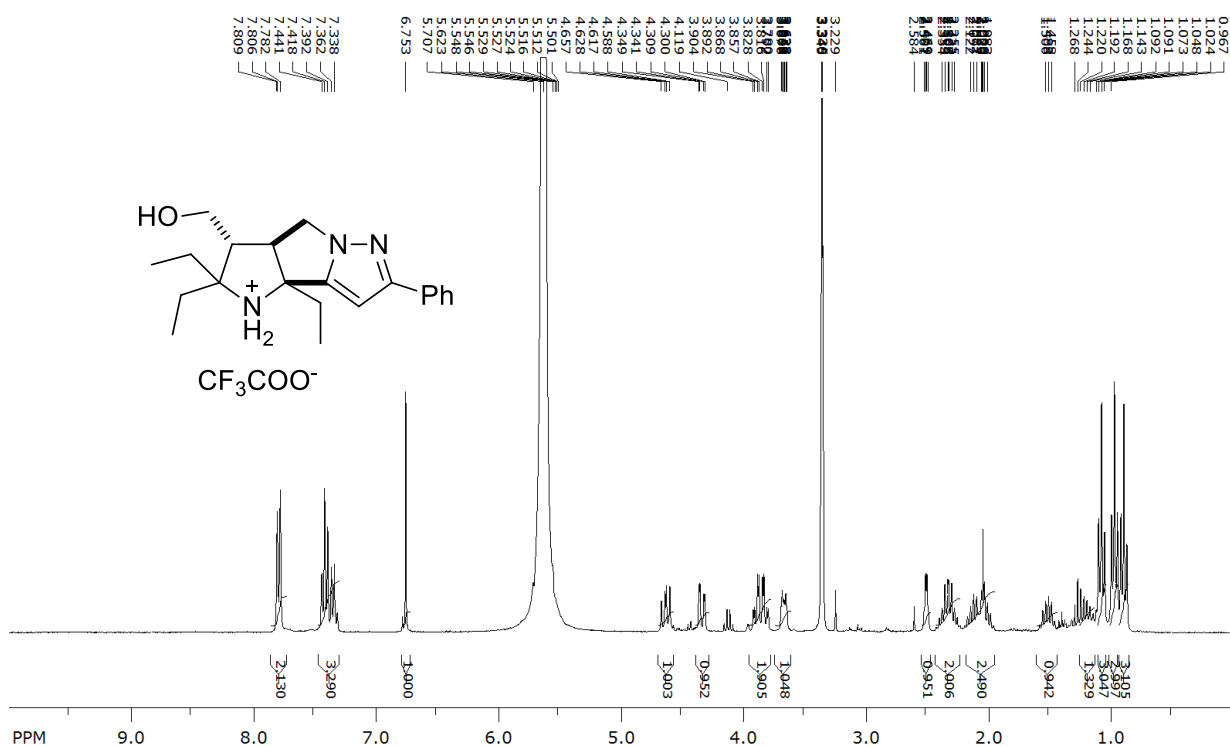


Figure S12. ^1H NMR (300 MHz, CD_3OD , $\text{Zn}/\text{CF}_3\text{COOH}$) of 3b,5,5-triethyl-6-(hydroxymethyl)-2-phenyl-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2-*b*]pyrazol-4-oxyl (9c)



IR spectra

Figure S13. IR (KBr) of 2,2,5-triethyl-3,4-bis(hydroxymethyl)-5-((trimethylsilyl)ethynyl)pyrrolidin-1-oxyl (2d)

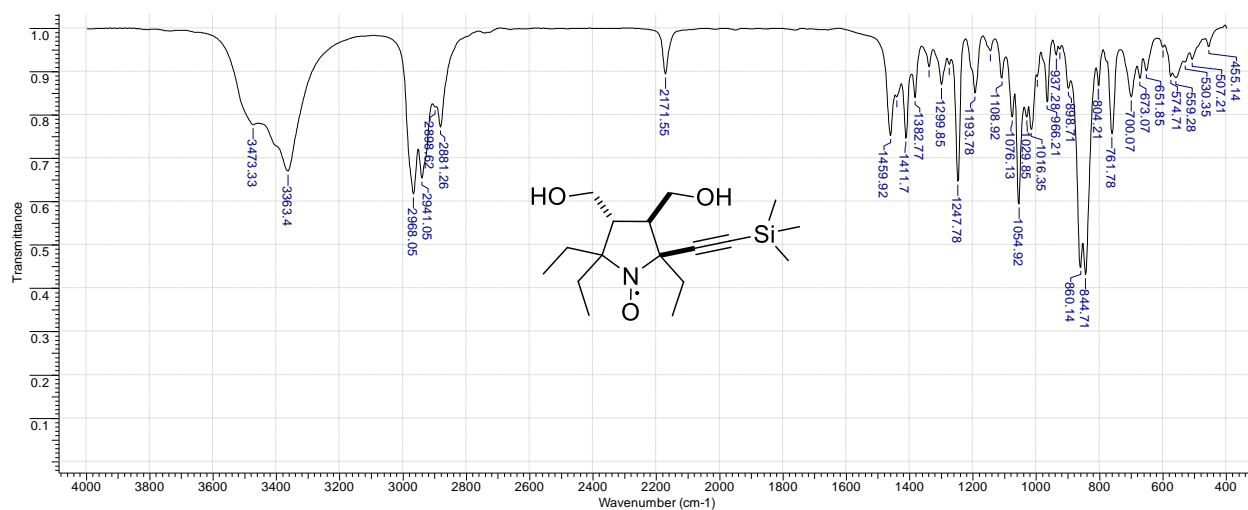


Figure S14. IR (neat) of 2-(3-(benzyloxy)prop-1-yn-1-yl)-2,5,5-triethyl-3,4-bis(hydroxymethyl)pyrrolidin-1-oxyl (2e)

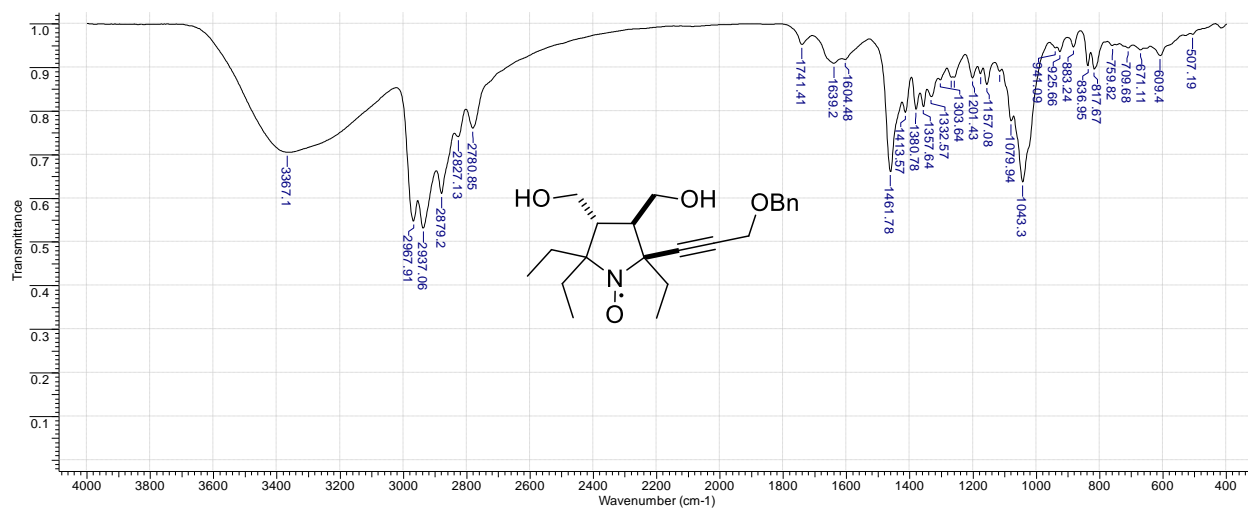


Figure S15. IR (neat) of 2-(3-(dimethylamino)prop-1-yn-1-yl)-2,5,5-triethyl-3,4-bis(hydroxymethyl)pyrrolidin-1-oxyl (2f)

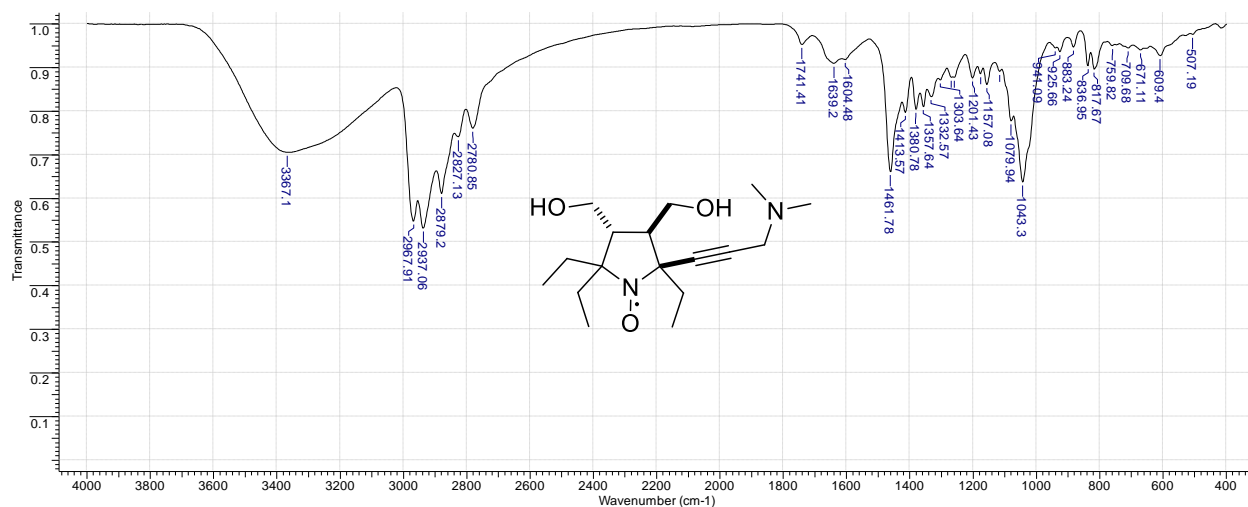


Figure S16. IR (KBr) of 2,2,5-triethyl-5-ethynyl-3,4-bis(((methylsulfonyl)oxy)methyl)pyrrolidin-1-oxyl (3a)

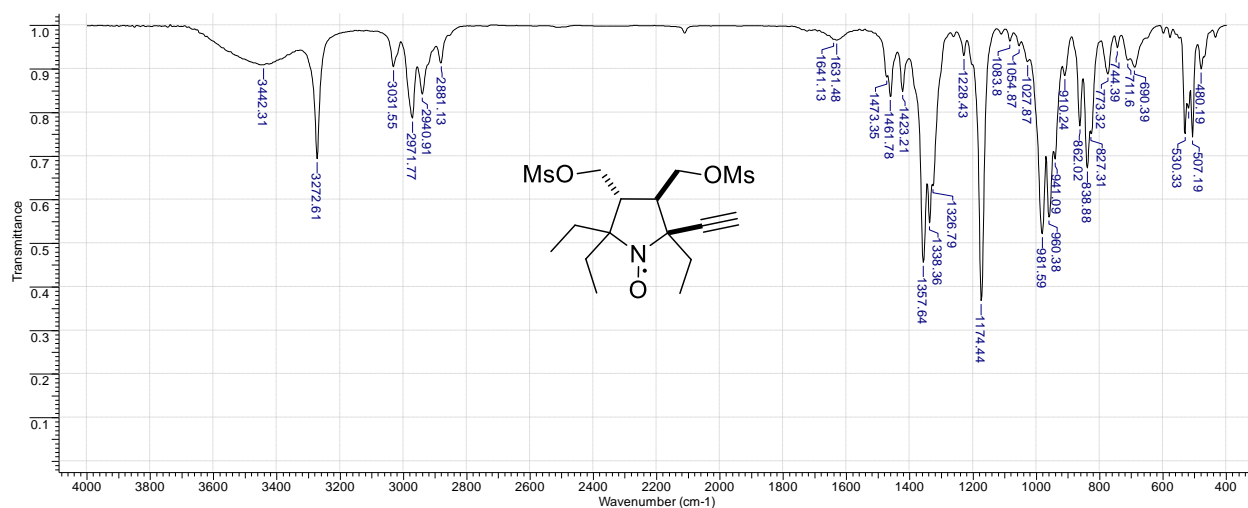


Figure S17. IR (neat) of 2,2,5-triethyl-3,4-bis(((methylsulfonyl)oxy)methyl)-5-(phenylethynyl)pyrrolidin-1-oxyl (3b)

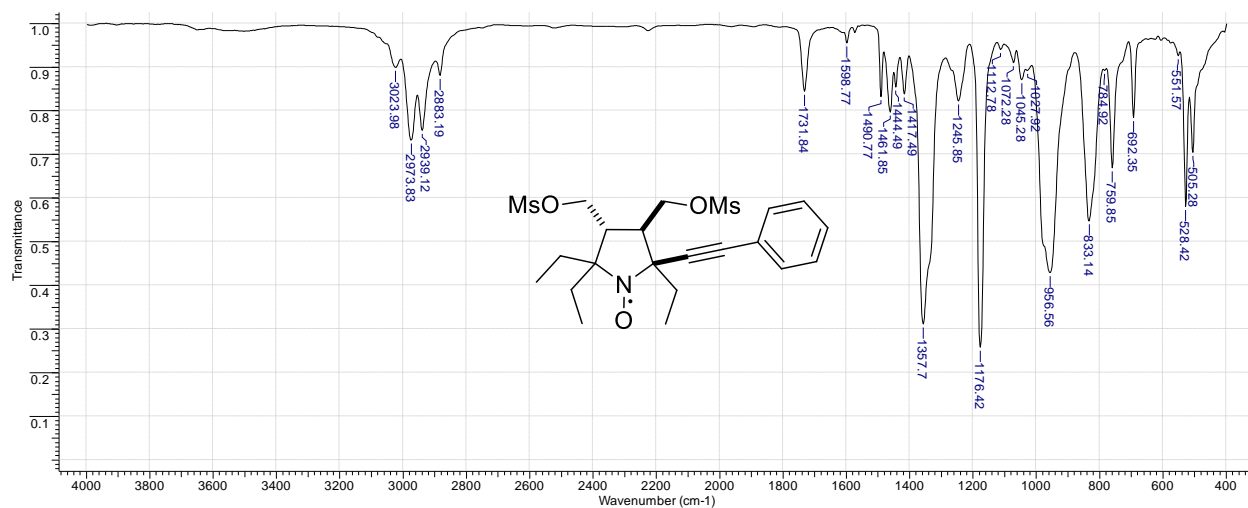


Figure S18. IR (neat) of 2,2,5-triethyl-3,4-bis(((methylsulfonyl)oxy)methyl)-5-(3-((methylsulfonyl)oxy)prop-1-yn-1-yl)pyrrolidin-1-oxyl (3c)

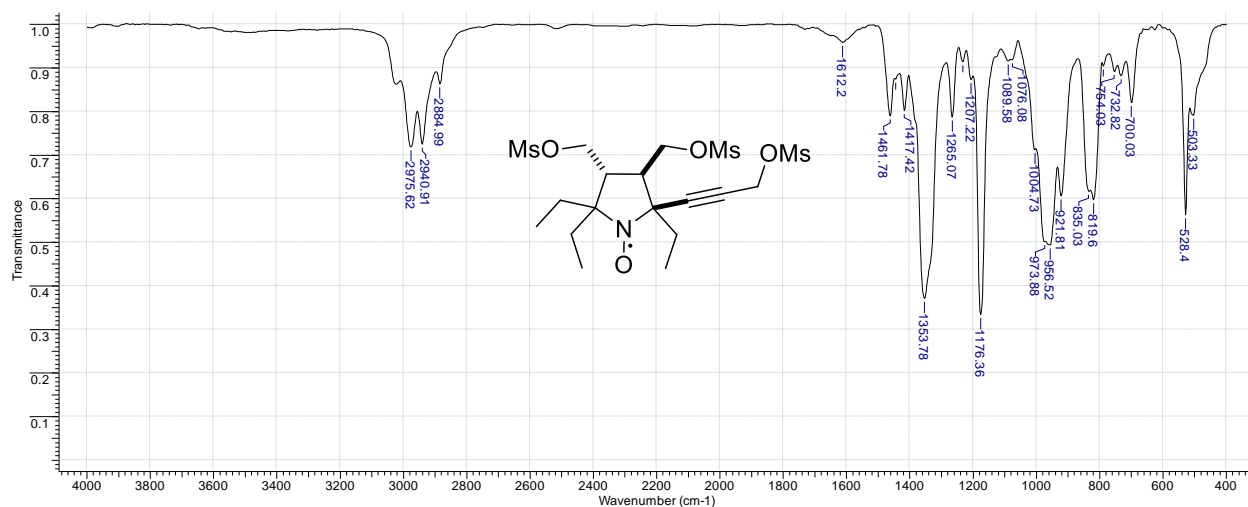


Figure S19. IR (neat) of 2,2,5-triethyl-3,4-bis(((methylsulfonyl)oxy)methyl)-5-((trimethylsilyl)ethynyl)pyrrolidin-1-oxyl (3d)

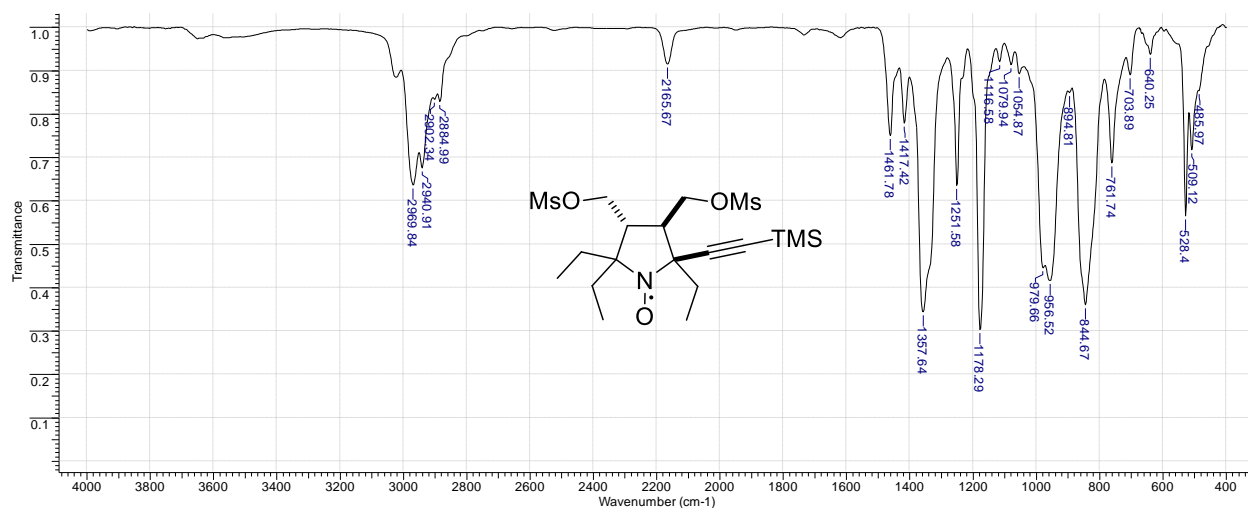


Figure S20. IR (neat) of 2-(3-(benzyloxy)prop-1-yn-1-yl)-2,5,5-triethyl-3,4-bis(((methylsulfonyl)oxy)methyl)pyrrolidin-1-oxyl (3e)

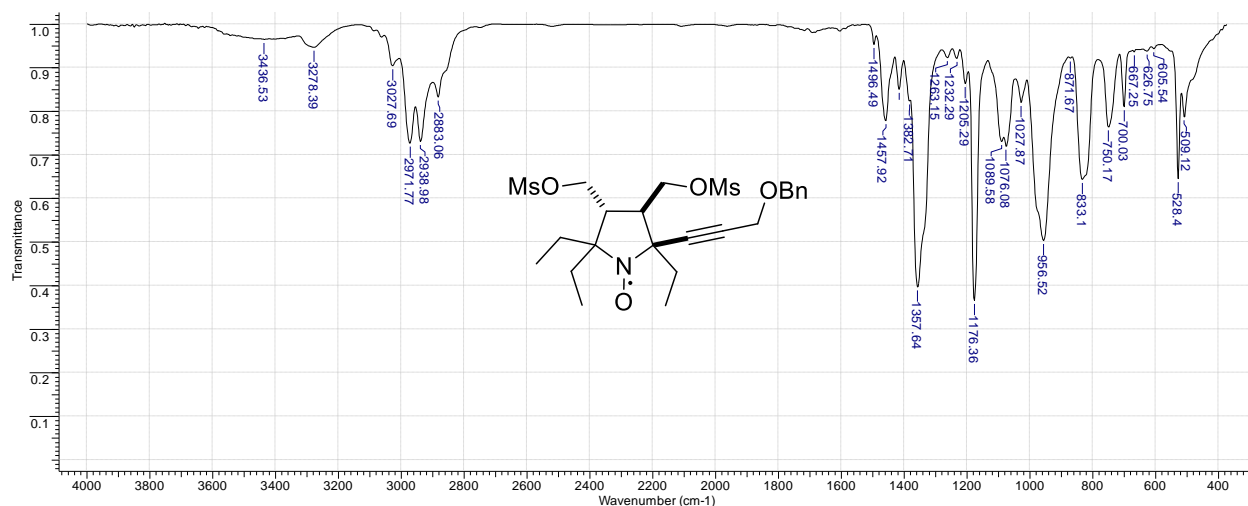


Figure S21. IR (neat) of 2-(3-(dimethylamino)prop-1-yn-1-yl)-2,5,5-triethyl-3,4-bis(((methylsulfonyl)oxy)methyl)pyrrolidin-1-oxyl (3f)

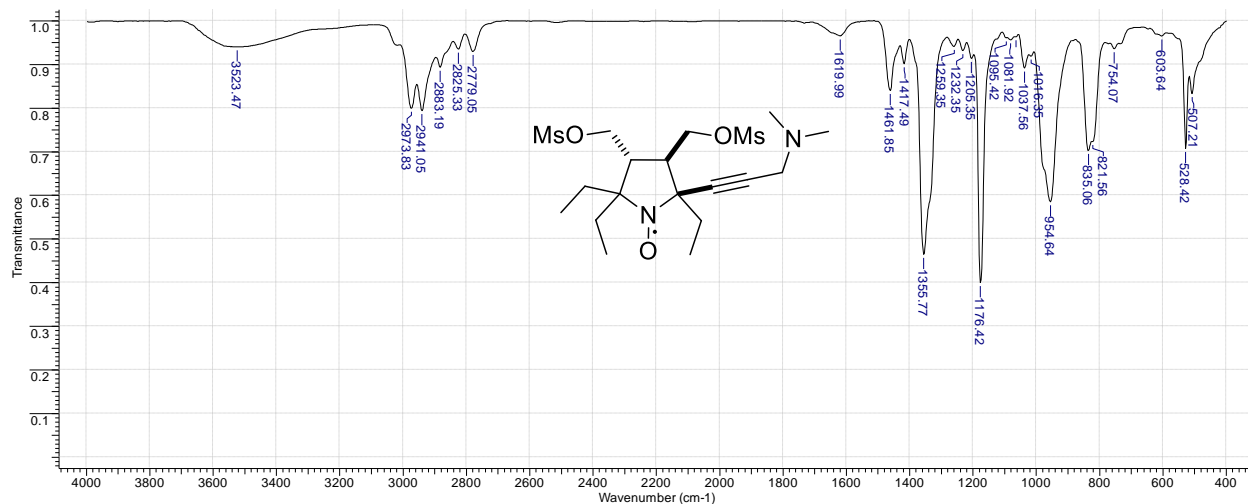


Figure S22. IR (KBr) of 6-(azidomethyl)-3b,5,5-triethyl-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2-c][1,2,3]triazol-4-oxyl (4a)

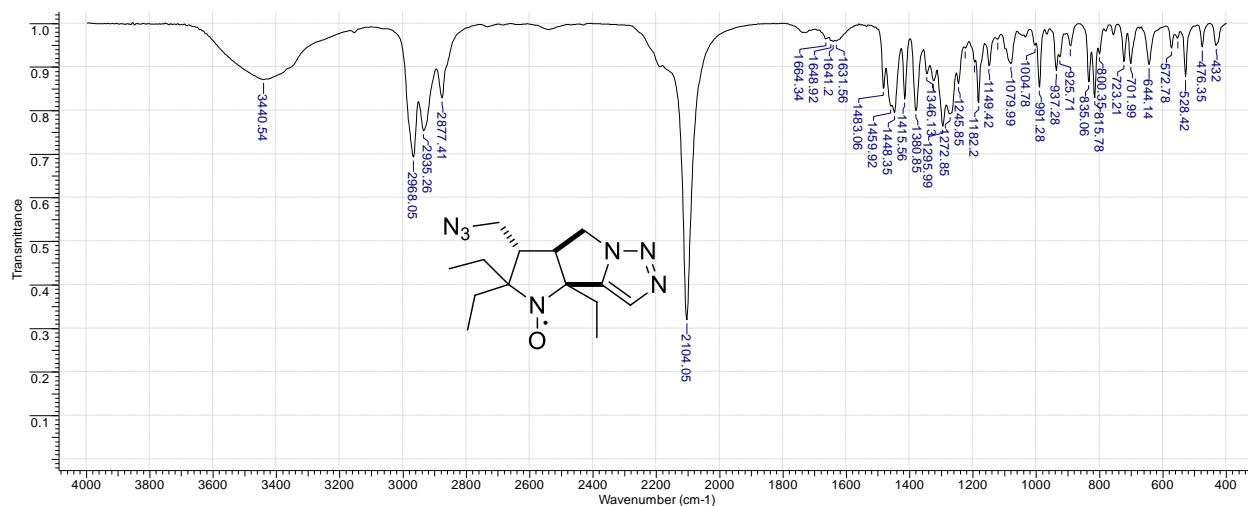


Figure S23. IR (KBr) of 6-(azidomethyl)-3b,5,5-triethyl-3-phenyl-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2-c][1,2,3]triazol-4-oxyl (4b)

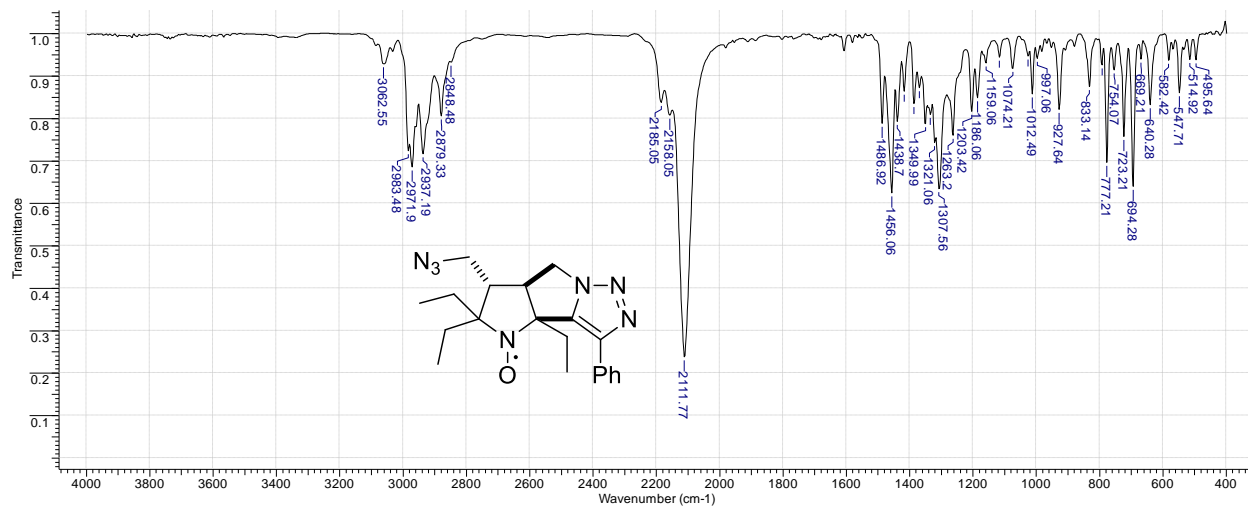


Figure S24. IR (KBr) of 3,6-bis(azidomethyl)-3b,5,5-triethyl-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2-c][1,2,3]triazol-4-oxyl (4c)

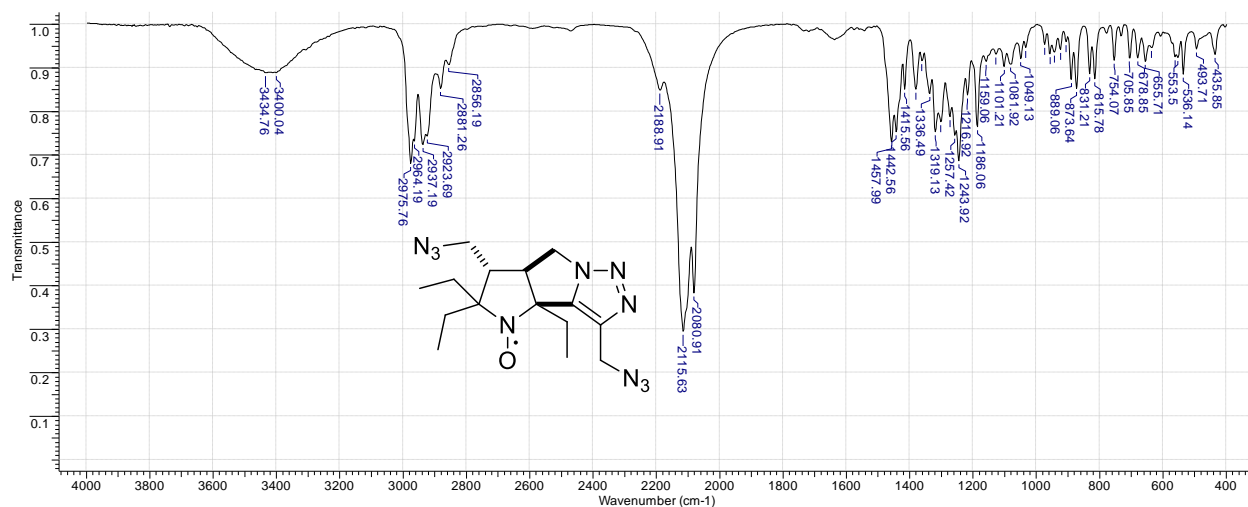


Figure S25. IR (KBr) of 6-(azidomethyl)-3b,5,5-triethyl-3-(trimethylsilyl)-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2-c][1,2,3]triazol-4-oxyl (4d)

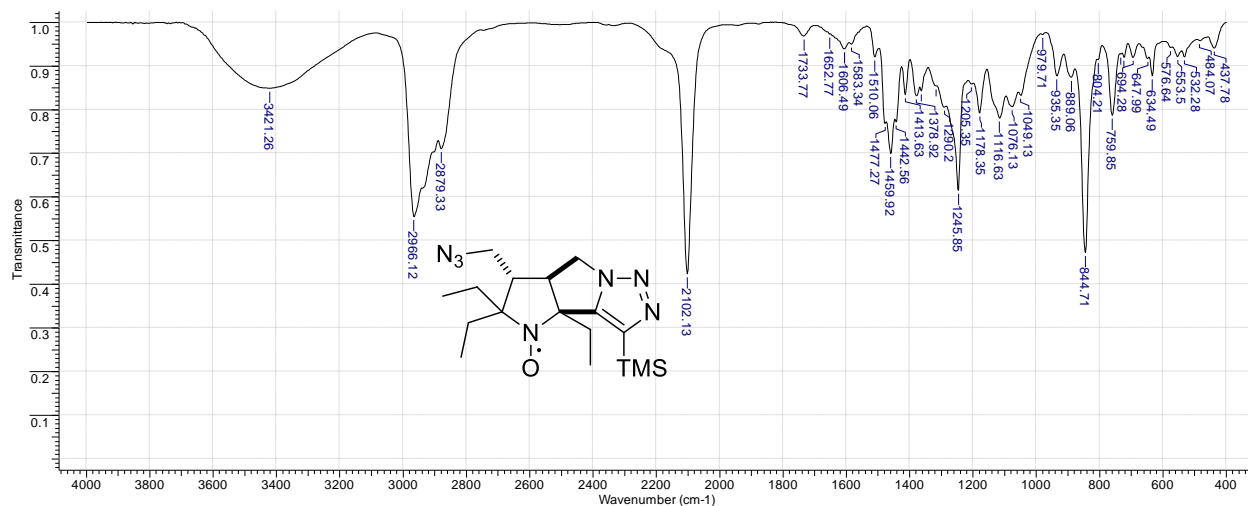


Figure S26. IR (neat) of 6-(azidomethyl)-3-((benzyloxy)methyl)-3b,5,5-triethyl-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2-c][1,2,3]triazol-4-oxyl (4e)

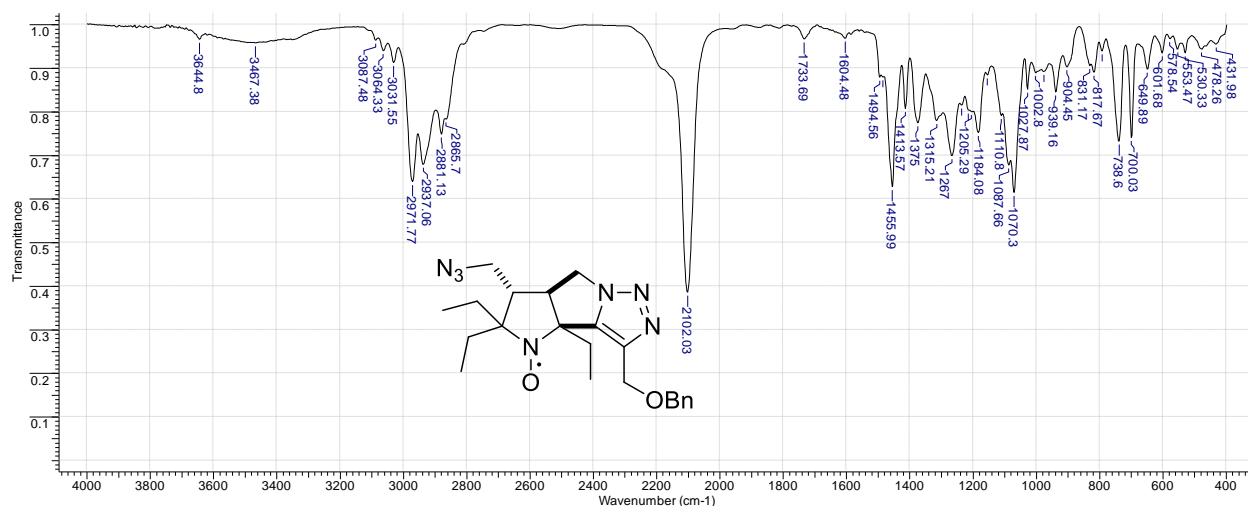


Figure S27. IR (neat) of 6-(azidomethyl)-3-((dimethylamino)methyl)-3b,5,5-triethyl-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2-c][1,2,3]triazol-4-oxyl (4f)

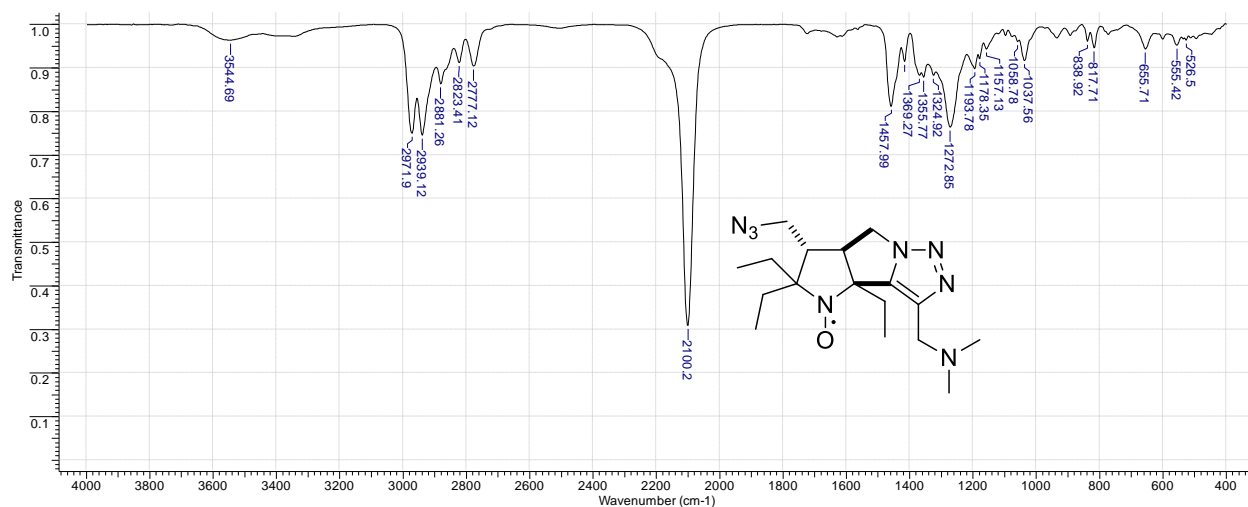


Figure S28. IR (neat) of 3,4-bis(acetoxymethyl)-2,2,5-triethyl-5-ethynylpyrrolidin-1-oxyl (5)

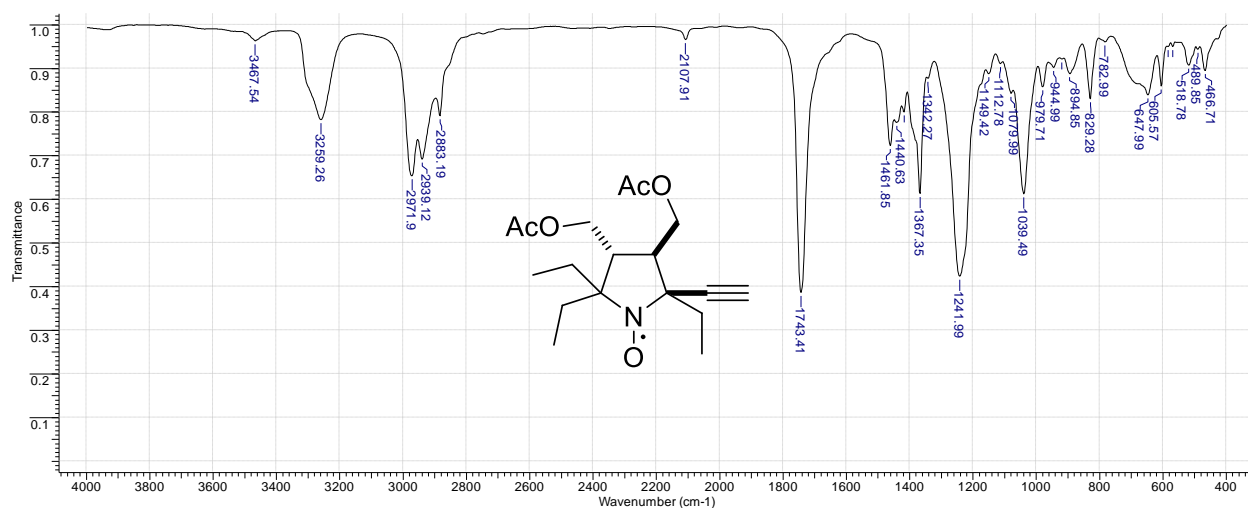


Figure S29. IR (neat) of 3,4-bis(acetoxymethyl)-2,2,5-triethyl-5-(3-oxo-3-phenylprop-1-yn-1-yl)pyrrolidin-1-oxyl (6a)

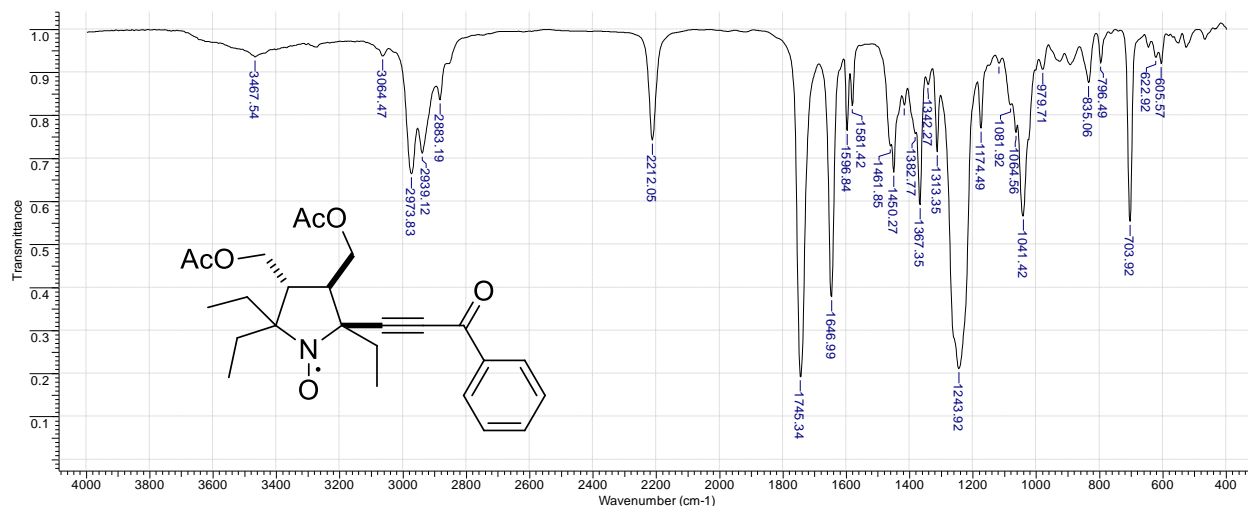


Figure S30. IR (neat) of 2,2,5-triethyl-3,4-bis(((methylsulfonyl)oxy)methyl)-5-(3-oxo-3-phenylprop-1-yn-1-yl)pyrrolidin-1-oxyl (6b)

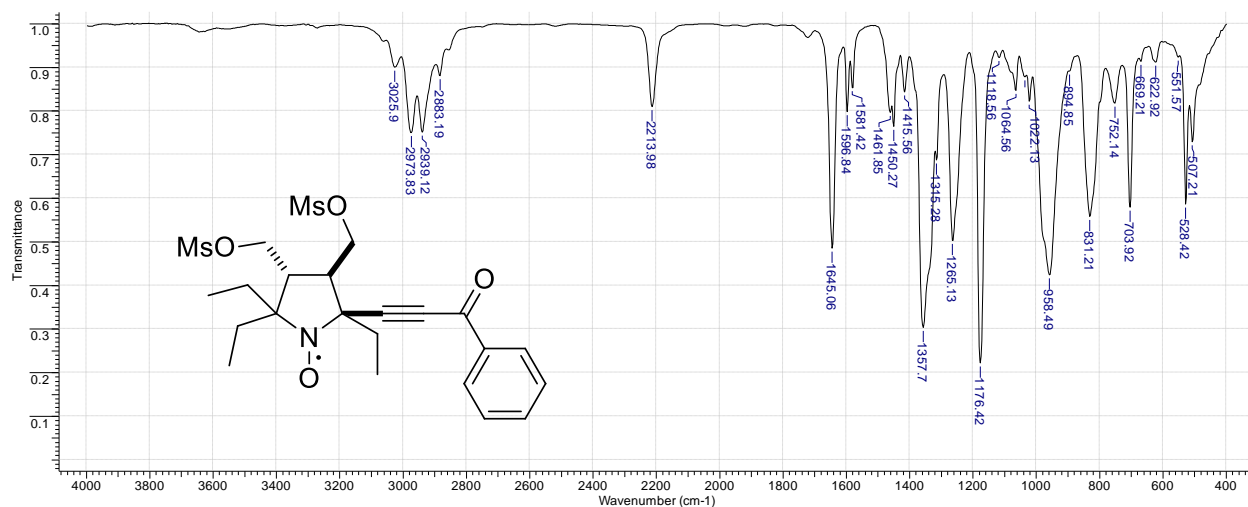


Figure S31. IR (KBr) of (Z)-2,2,6a-triethyl-3-(hydroxymethyl)-6-(2-oxoethylidene)hexahydro-1H-furo[3,4-b]pyrrol-1-oxyl (8)

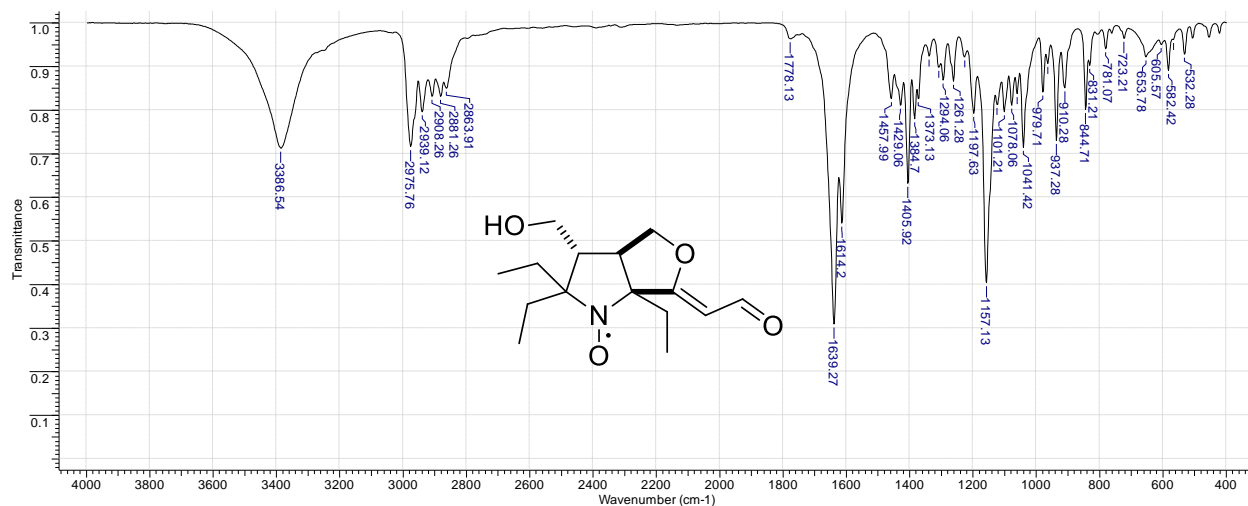


Figure S32. IR (neat) 2,2,5-triethyl-3,4-bis(hydroxymethyl)-5-(3-phenyl-1H-pyrazol-5-yl)pyrrolidin-1-oxyl (9a)

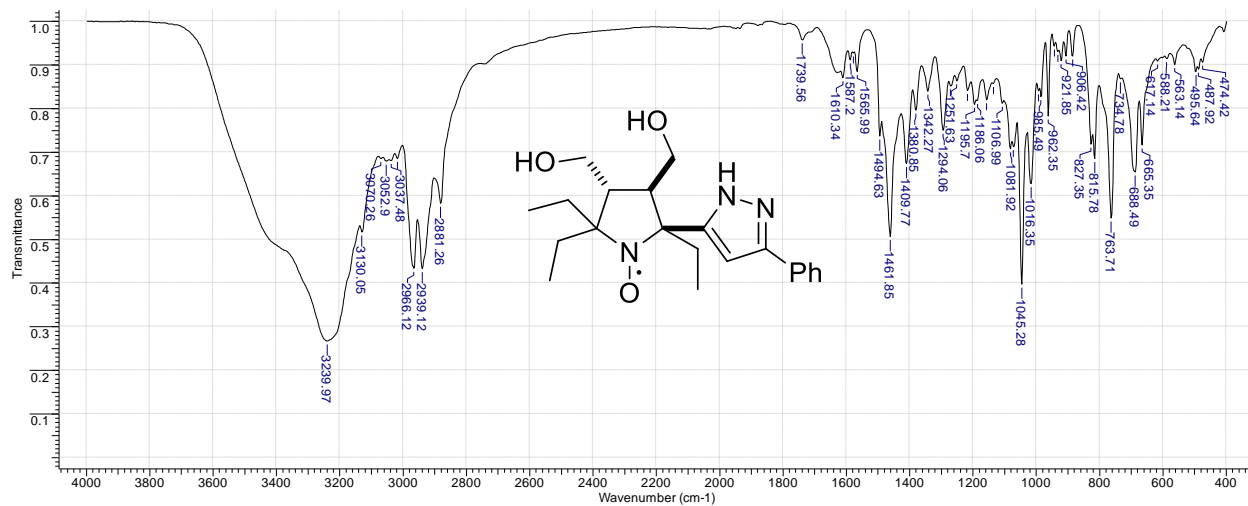


Figure S33. IR (neat) 3b,5,5-triethyl-6-(((methylsulfonyl)oxy)methyl)-2-phenyl-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2-*b*]pyrazol-4-oxyl (9b)

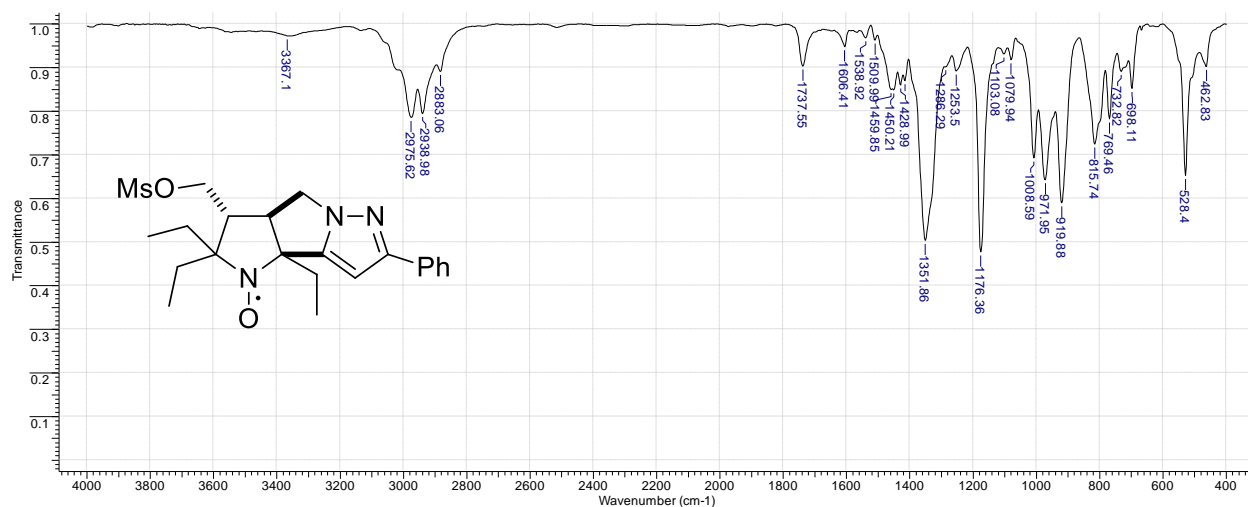
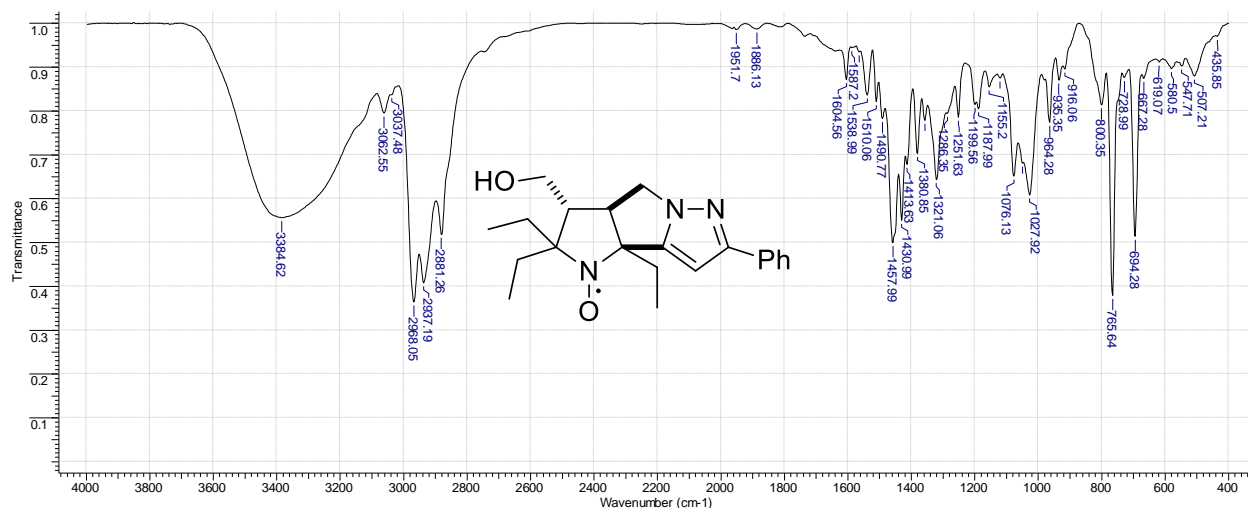


Figure S34. IR (KBr) 3b,5,5-triethyl-6-(hydroxymethyl)-2-phenyl-3b,4,5,6,6a,7-hexahydropyrrolo[2',3':3,4]pyrrolo[1,2-*b*]pyrazol-4-oxyl (9c)



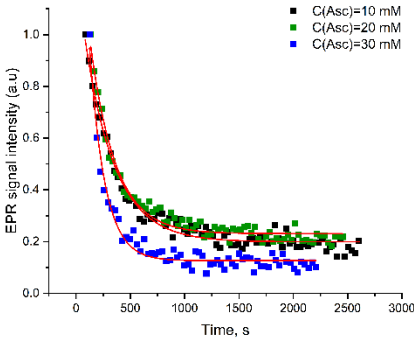
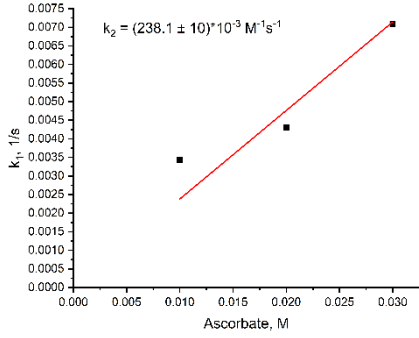
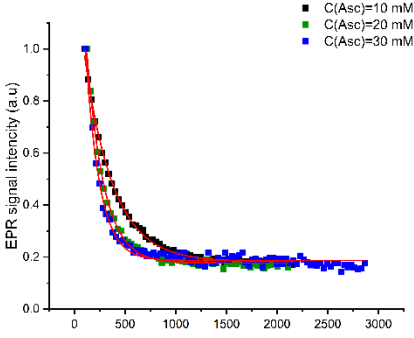
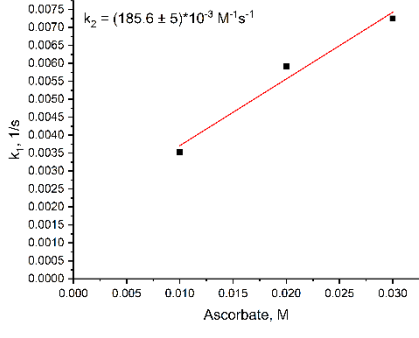
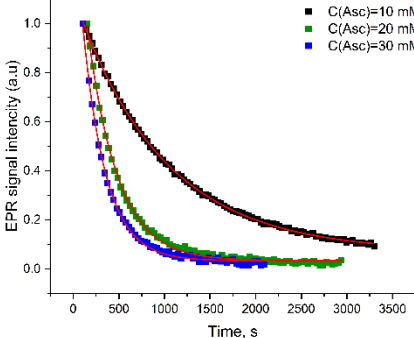
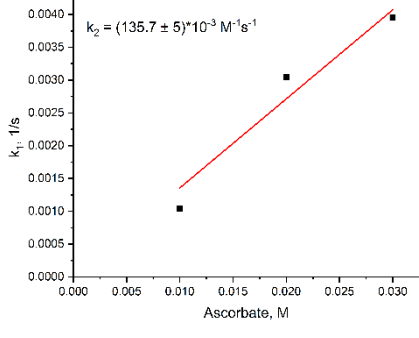
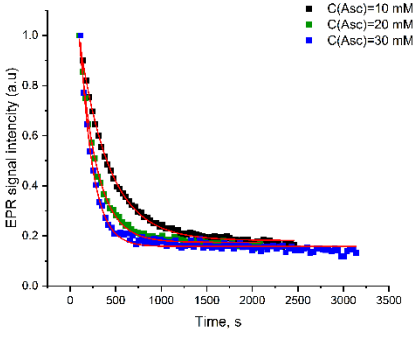
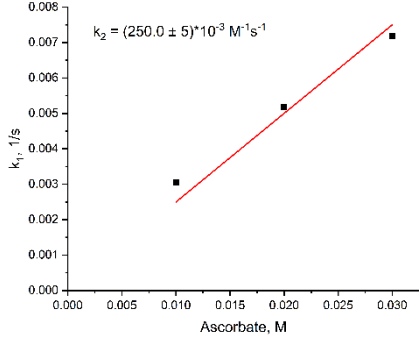
EPR measurements

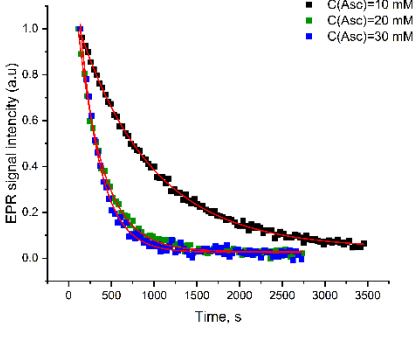
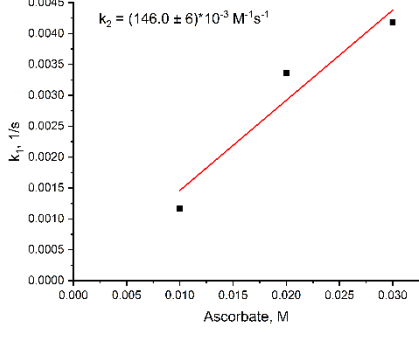
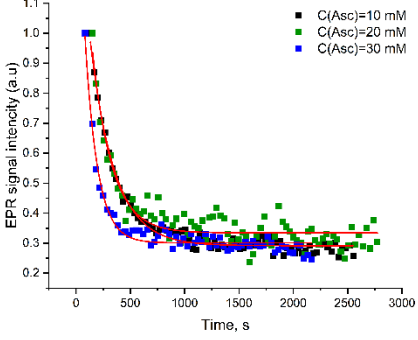
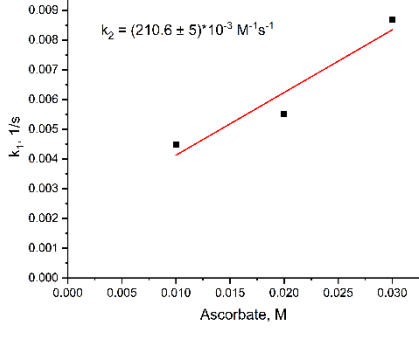
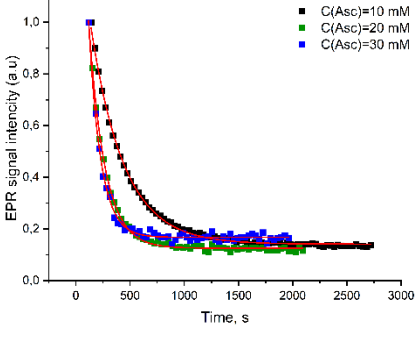
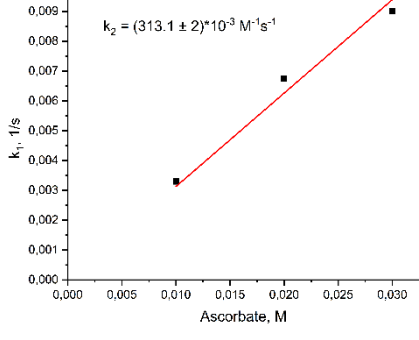
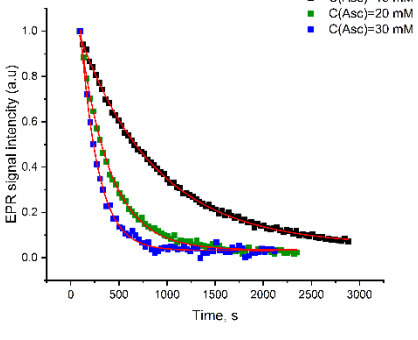
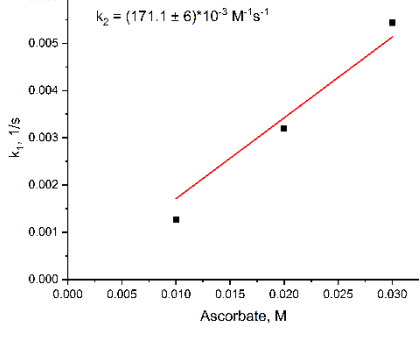
CW EPR spectra were recorded in the X-band (≈ 9.87 GHz) using commercial Bruker Elexsys E 540 spectrometer (Bruker Corporation, Billerica, MA, USA). The measurements were performed in glass capillaries (100 μ L) with the following spectrometer settings: modulation amplitude – 1 G; microwave power – 2 mW. Simulations of solution electron spin resonance lines were carried out in the EasySpin software (6.0.0), which is available at <http://www.easyspin.org>. EPR spectra were recorded for 0.4 mM buffer solutions of nitroxyl radicals.

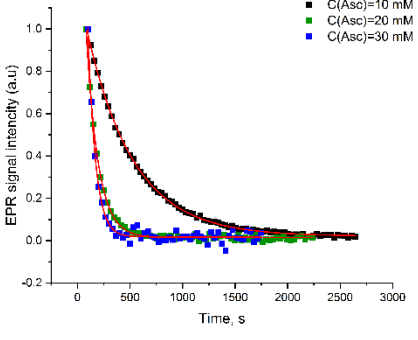
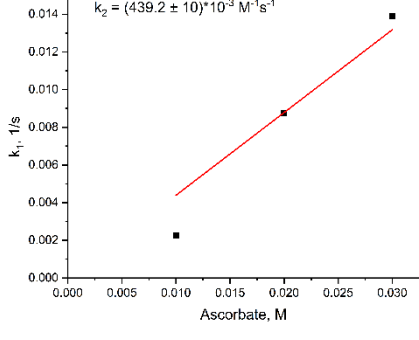
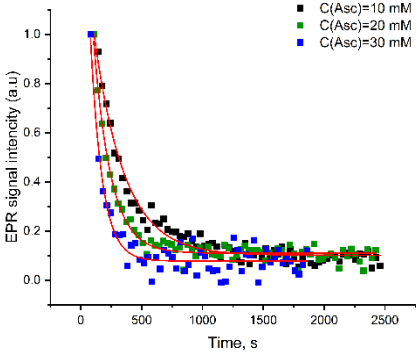
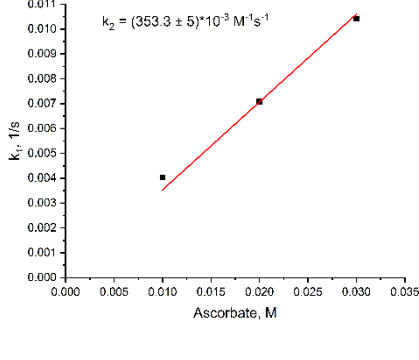
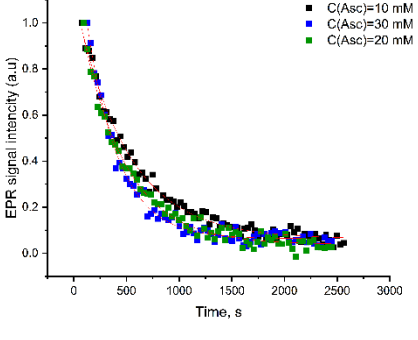
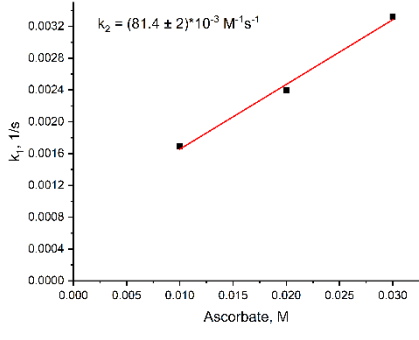
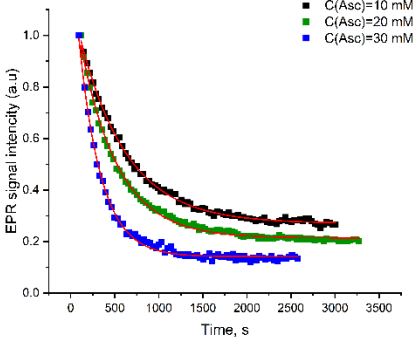
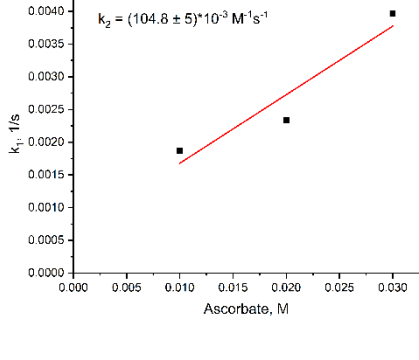
The kinetics measurements were carried out using following general procedure. Fresh stock solutions of ascorbic acid (40, 80, 120 mM), glutathione (GSH) (8.0 mM), and a nitroxide (0.4 mM) in 10 mM phosphate buffer were prepared. The pH of the solutions was adjusted to 7.5 with NaOH (0.1 M solution). The stock solutions were carefully and quickly mixed using a stirrer Vortex V-1 Plus to achieve a concentration of 0.2 mM of the nitroxide, 10, 20 and 30 mM of ascorbate and 2 mM of glutathione. The mixture was taken into an EPR glass capillary. The sample was immediately placed into the resonator of the X-band CW EPR spectrometer and a series of spectra were recorded automatically one after another at equal intervals. Double integrals of the whole spectra were used to follow the nitroxide reduction. The data are plotted in Table S1 (see below). The analysis of the data was performed on the basis of previously published data on kinetics and mechanism of reduction of similar sterically shielded nitroxides in ascorbate–glutathione mixtures [S3]. The large excess of ascorbate allowed to process EPR signal decay rate as pseudo-first order reaction kinetics. The rate constants of the second-order reaction were determined by extracting the slope from the plot of the rate constant k_1 versus concentration of ascorbate. The measurement error was calculated based on the three kinetic points.

S3. Bobko, A. A.; Kirilyuk, I. A.; Grigor'ev, I. A.; Zweier, J. L.; Khramtsov, V. V. Reversible reduction of nitroxides to hydroxylamines: Roles for ascorbate and glutathione. *Free Radical Biol. Med.* **2006**, 42 (3), 404–412. <https://doi.org/10.1016/j.freeradbiomed.2006.11.007>.

Table S1. Reduction rate constants of nitroxide 2a–f, 4a–f, 9c

Nitroxide	$k_2 \cdot 10^3, \text{M}^{-1} \text{s}^{-1}$	Kinetic curves	k_1
2a	238.1 ± 10		
2b	185.6 ± 5		
2c	135.7 ± 5		
2d	250.0 ± 5		

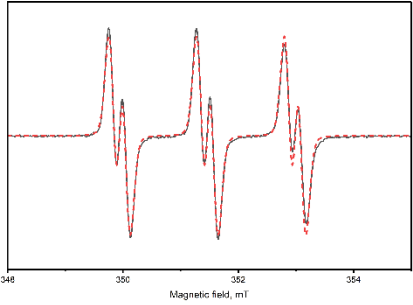
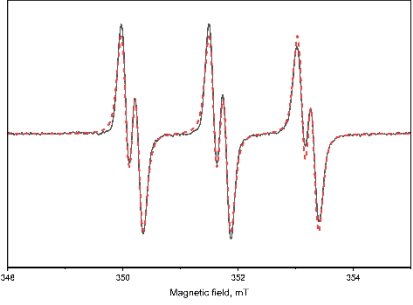
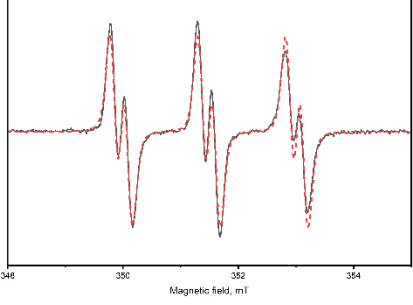
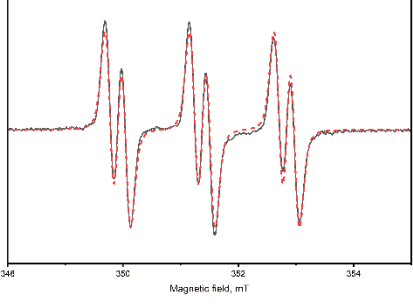
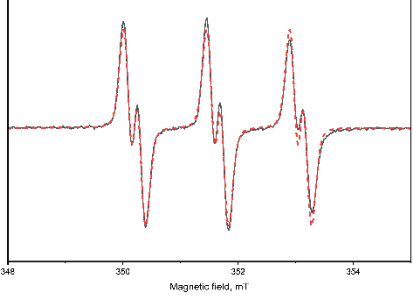
Nitroxide	$k_2 \cdot 10^3, \text{M}^{-1} \text{s}^{-1}$	Kinetic curves	k_1
2e	146.0 ± 6		
2f	210.6 ± 5		
4a	313.1 ± 2		
4b	171.1 ± 6		

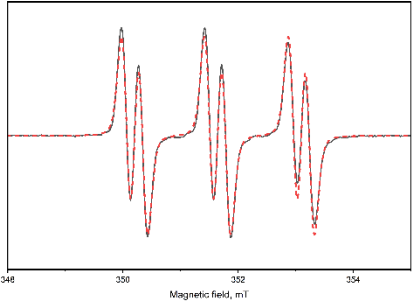
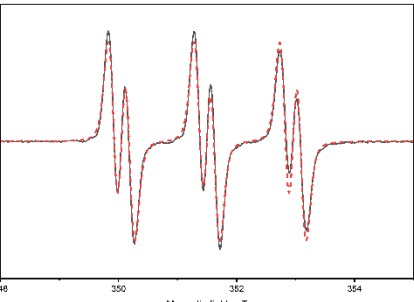
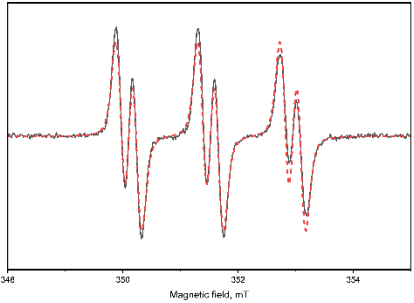
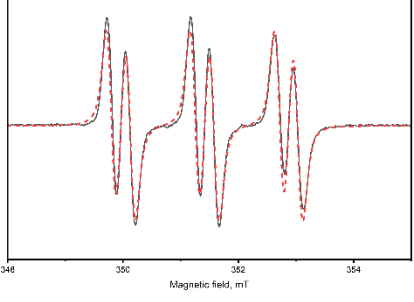
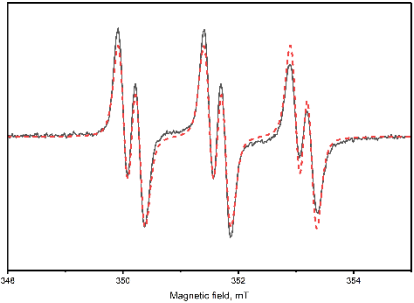
Nitroxide	$k_2 \cdot 10^3, \text{M}^{-1} \text{s}^{-1}$	Kinetic curves	k_1
4c	439.2 ± 10		
4d	353.3 ± 5		
4e	81.4 ± 1		
4f	104.8 ± 5		

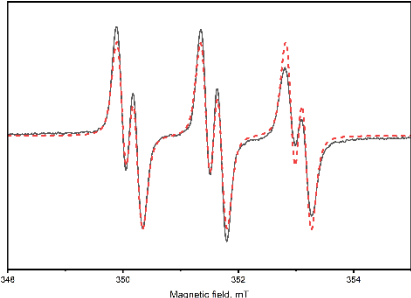
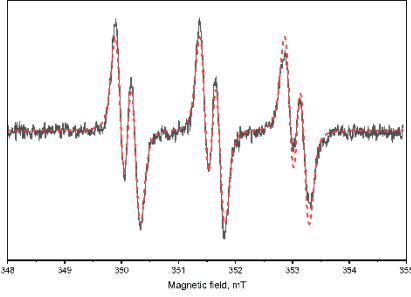
Nitroxide	$k_2 \cdot 10^3, \text{M}^{-1} \text{s}^{-1}$	Kinetic curves	k_1
9c	85.2 ± 1		

Table S2. EPR spectral parameters of nitroxides 2a–f, 4a–f, 9a–c

Nitroxide	a_N, mT (± 0.005)	a_H, mT (± 0.005)	Line width, mT (± 0.001)	Spectrum
2a	1.53	0.23	0.006	
2b	1.53	0.21	0.006	
2c	1.54	0.21	0.006	

Nitroxide	a_N , mT (± 0.005)	a_H , mT (± 0.005)	Line width, mT (± 0.001)	Spectrum
2d	1.53	0.21	0.006	
2e	1.53	0.21	0.006	
2f	1.53	0.23	0.006	
4a	1.47	0.26	0.007	
4b	1.45	0.22	0.007	

Nitroxide	a_N , mT (± 0.005)	a_H , mT (± 0.005)	Line width, mT (± 0.001)	Spectrum
4c	1.45	0.27	0.007	
4d	1.45	0.26	0.007	
4e	1.43	0.26	0.007	
4f	1.46	0.31	0.006	
9a	1.50	0.28	0.007	

Nitroxide	a_N , mT (± 0.005)	a_H , mT (± 0.005)	Line width, mT (± 0.001)	Spectrum
9b	1.47	0.26	0.007	
9c	1.49	0.25	0.007	

X-ray crystallographic analysis

The X-ray diffraction experiments were carried out on a Bruker KAPPA APEX II diffractometer (graphite-monochromated Mo K α radiation). Reflection intensities were corrected for absorption by *SADABS2016/2* program [S4]. The structure was solved by direct methods using the *SHELXT2014/5* [S5] and refined by anisotropic (isotropic for all H atoms) full-matrix least-squares method against F^2 of all reflections by *SHELXL2018/3*[S6]. The positions of the hydrogen atoms were calculated geometrically and refined in a riding model except for **2d**, **8** and **9**. Asymmetric unit of **2d** includes four independent molecules and for one of them hydroxy hydrogens were localized from d-map and refined independently with O–H bond lengths restriction to 0.82 Å. The same procedure was done for hydroxyls of **6** and **9a** without any restriction of bond lengths. The details of experiment and structure refinement are given in Table S3.

Crystallographic data for **2d**, **4a–c**, **8**, **9a** have been deposited at the Crystallographic Data Centre as supplementary publication no. CCDC 2512649-2512654. Copy of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: +44 122 3336033 or e-mail: deposit@ccdc.cam.ac.uk; internet: www.ccdc.cam.ac.uk).

Table S3. Experimental and structure refinement details for 2d, 4a–c, 8, 9a

	2d	4a	4b	4c	8	9a
Chemical formula	C ₁₇ H ₃₂ NO ₃ Si	C ₁₄ H ₂₂ N ₇ O	C ₂₀ H ₂₆ N ₇ O	C ₁₅ H ₂₃ N ₁₀ O	C ₁₅ H ₂₄ NO ₄	C ₂₁ H ₃₀ N ₃ O ₃
M_r	326.52	304.38	380.48	359.43	282.35	372.48
Crystal system, space group	Triclinic, $P\bar{1}$	Monoclinic, $P2_1$	Monoclinic, $P2_1/n$	Monoclinic, $P2_1/c$	Monoclinic, $P2_1/n$	Monoclinic, $P2_1/n$
Temperature (K)	296	296	296	296	296	200
a, b, c (Å)	12.4707(5) 17.5991(8) 19.5933(9)	7.4655(5) 11.8859(6) 9.1833(5)	8.403(3) 8.881(3) 27.00(1)	12.2895(7), 9.5375(4), 15.8665(7)	8.0418(7), 12.055(1), 15.989(2)	14.501(3), 10.311(2), 14.717(3)
α, β, γ (°)	82.553(2) 79.474(2) 71.963(2)	90, 95.219(2), 90	90, 93.113(10), 90	90, 98.802(2), 90	90, 102.711(4), 90	90, 115.511(6), 90
V (Å ³)	4007.8 (3)	811.49 (8)	2012.0 (13)	1837.83 (15)	1512.0(3)	1985.9(7)
Z	8	2	4	4	4	4

$F(000)$	1432	326	812	764	612	804
D_x (Mg m ⁻³)	1.082	1.246	1.256	1.299	1.240	1.246
μ (mm ⁻¹)	0.13	0.09	0.08	0.09	0.09	0.08
Crystal size (mm)	0.80 × 0.40 × 0.20	0.72 × 0.41 × 0.31	0.41 × 0.24 × 0.07	0.68 × 0.58 × 0.25	0.29 × 0.13 × 0.04	0.40 × 0.10 × 0.06
T_{\min}, T_{\max}	0.707, 0.745	0.877, 0.928	0.909, 0.959	0.897, 0.937	0.883, 0.958	0.901, 0.971
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	56190, 15904, 10265	14376, 4103, 3584	43855, 4848, 3551	30287, 4221, 3182	9999, 2661, 1428	23165, 3507, 2299
R_{int}	0.035	0.045	0.069	0.060	0.079	0.091
θ range (°)	1.6 - 26.1	2.7 - 28.5	2.8 - 28.0	2.9 - 27.5	3.1 - 25.1	3.3 - 25.1
Range of h, k, l	$h = -15 \rightarrow 15$ $k = -21 \rightarrow 21$ $l = -24 \rightarrow 24$	$h = -9 \rightarrow 10$ $k = -15 \rightarrow 15$ $l = -12 \rightarrow 12$	$h = -11 \rightarrow 11$ $k = -11 \rightarrow 11$ $l = -35 \rightarrow 35$	$h = -15 \rightarrow 15$ $k = -12 \rightarrow 12$ $l = -20 \rightarrow 20$	$h = -8 \rightarrow 9$ $k = -14 \rightarrow 13$ $l = -18 \rightarrow 19$	$h = -17 \rightarrow 17$ $k = -12 \rightarrow 12$ $l = -17 \rightarrow 17$
$R[F^2 > 2\sigma(F^2)], wR(F^2)$	0.064, 0.215	0.049, 0.140	0.049, 0.139	0.051, 0.165	0.077, 0.230	0.045, 0.111
Goof	1.00	1.05	1.02	1.02	1.00	1.00
No. of reflections	15904	4103	4848	4221	2661	3507
No. of parameters	840	202	253	238	188	259
No. of restraints	1	1	0	0	0	0
ρ_{\max}, ρ_{\min} (e Å ⁻³)	1.57, -0.49	0.29, -0.20	0.25, -0.18	0.35, -0.28	0.46, -0.18	0.18, -0.24
Flack parameter	—	0.0 (6)	—	—	—	—
CCDC number	2512649	2512650	2512651	2512652	2512653	2512654

S4. SADABS, v. 2008-1, Bruker AXS, Madison, WI, USA

S5. Sheldrick, G. M. SHELXT— Integrated Space-Group and Crystal-Structure Determination. *Acta Crystallogr., Sect. A*, **2015**, 71 (1), 3–8. <https://doi.org/10.1107/s2053273314026370>.

S6. Sheldrick, G. M. Crystal Structure Refinement With SHELXL. *Acta Crystallogr. Sect. C*. **2015**, 71 (1), 3–8. <https://doi.org/10.1107/s2053229614024218>.